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(12) **United States Patent**
Jennings

(10) **Patent No.:** **US 9,150,621 B2**
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(54) **MUTANT BACTERIAL GLYCOPROTEINS AND USES THEREOF**

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(75) Inventor: **Michael Paul Jennings**, Brisbane (AU)

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(73) Assignee: **The University of Queensland**, Queensland (AU)

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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§ 371 (c)(1),
(2), (4) Date: **Jul. 12, 2011**

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Aug. 28, 2008 (AU) 2008904429

(51) **Int. Cl.**

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A61K 39/095	(2006.01)
A61K 38/00	(2006.01)
C07K 16/22	(2006.01)
C12N 9/06	(2006.01)
C07K 16/12	(2006.01)
C12P 21/00	(2006.01)

(52) **U.S. Cl.**

CPC **C07K 14/22** (2013.01); **A61K 39/095** (2013.01); **C07K 16/1217** (2013.01); **C12N 9/0044** (2013.01); **C12P 21/005** (2013.01); **C12Y 107/02001** (2013.01); **A61K 38/00** (2013.01)

(58) **Field of Classification Search**

None
See application file for complete search history.

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Primary Examiner — Oluwatosin Ogunbiyi

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(57) **ABSTRACT**

The present invention relates to the use of mutant glycoproteins from pathogenic bacteria lacking one or more phosphocholine and/or glycosylation post-translational modifications as immunogens. These post-translational modifications act as masking structures that elicit an immune response which does not confer protection on an infected individual. The removal or modification of these masking structures alters the protein such that it elicits a stronger immune response to the protein and/or the bacterial pathogen. Particular examples are pilin proteins and nitrite reductase glycoproteins of *Neisseria* bacteria.

10 Claims, 21 Drawing Sheets

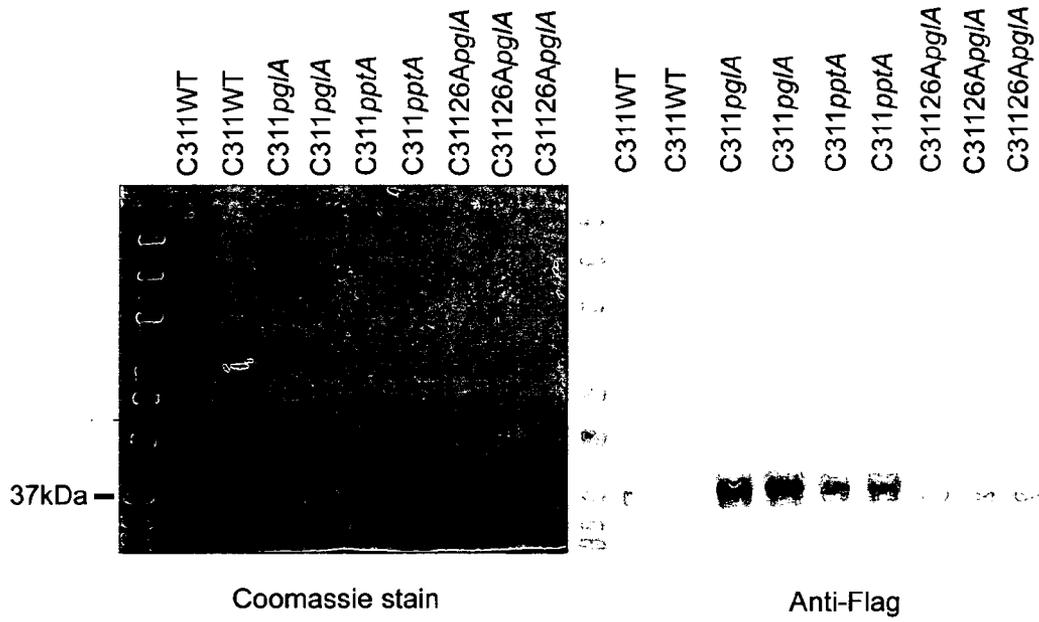


FIG. 1

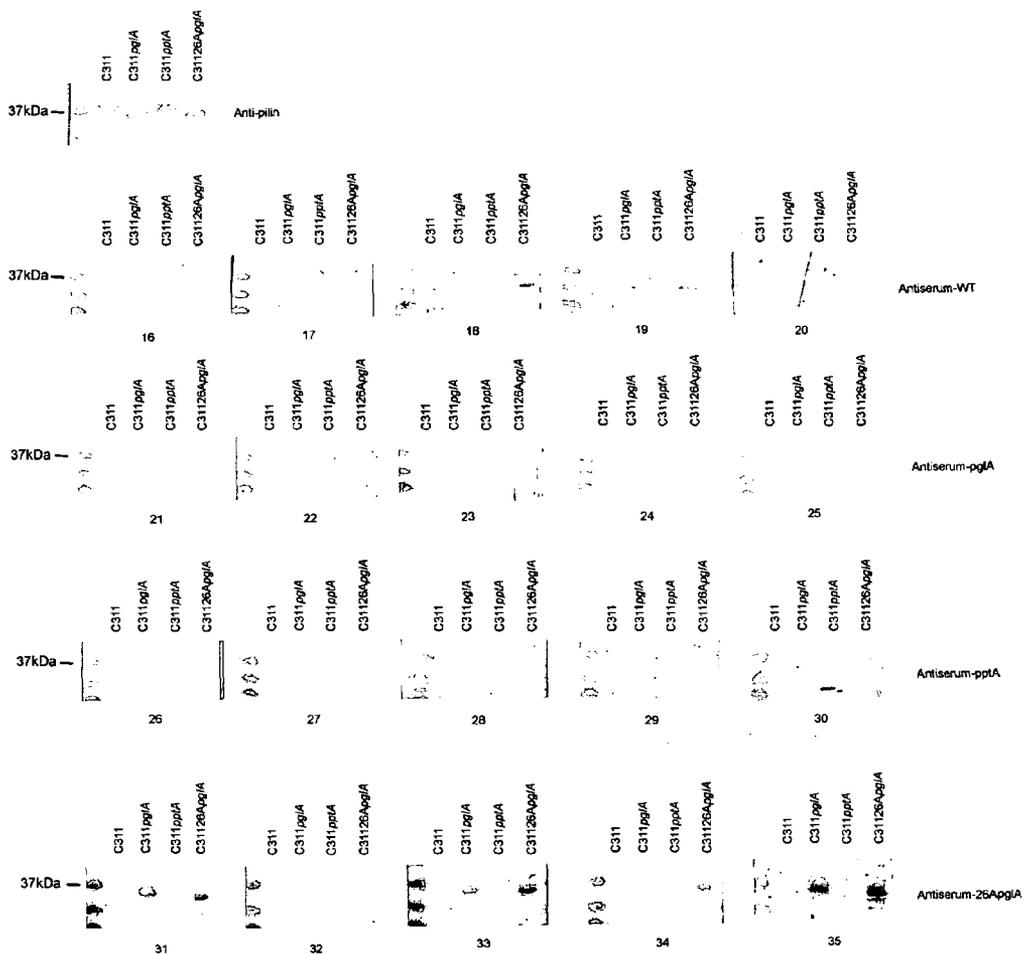


FIG. 2

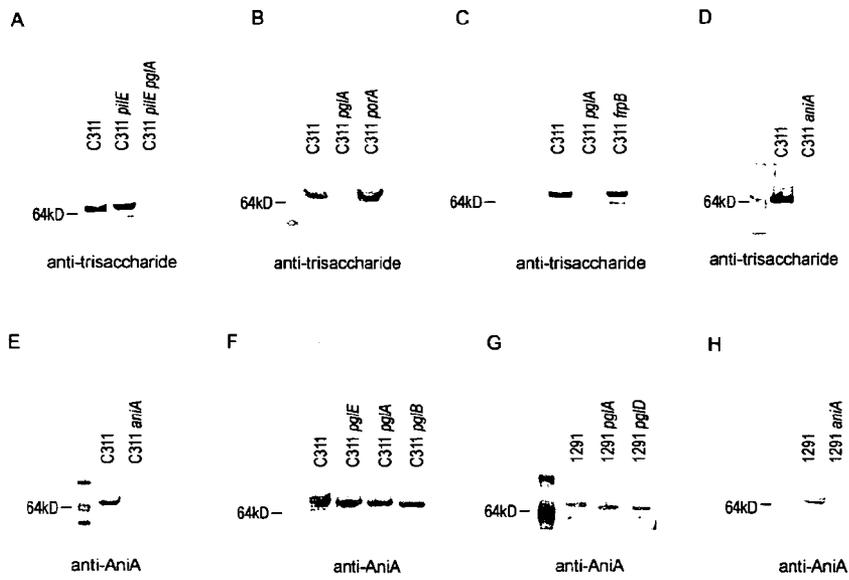


FIG. 3

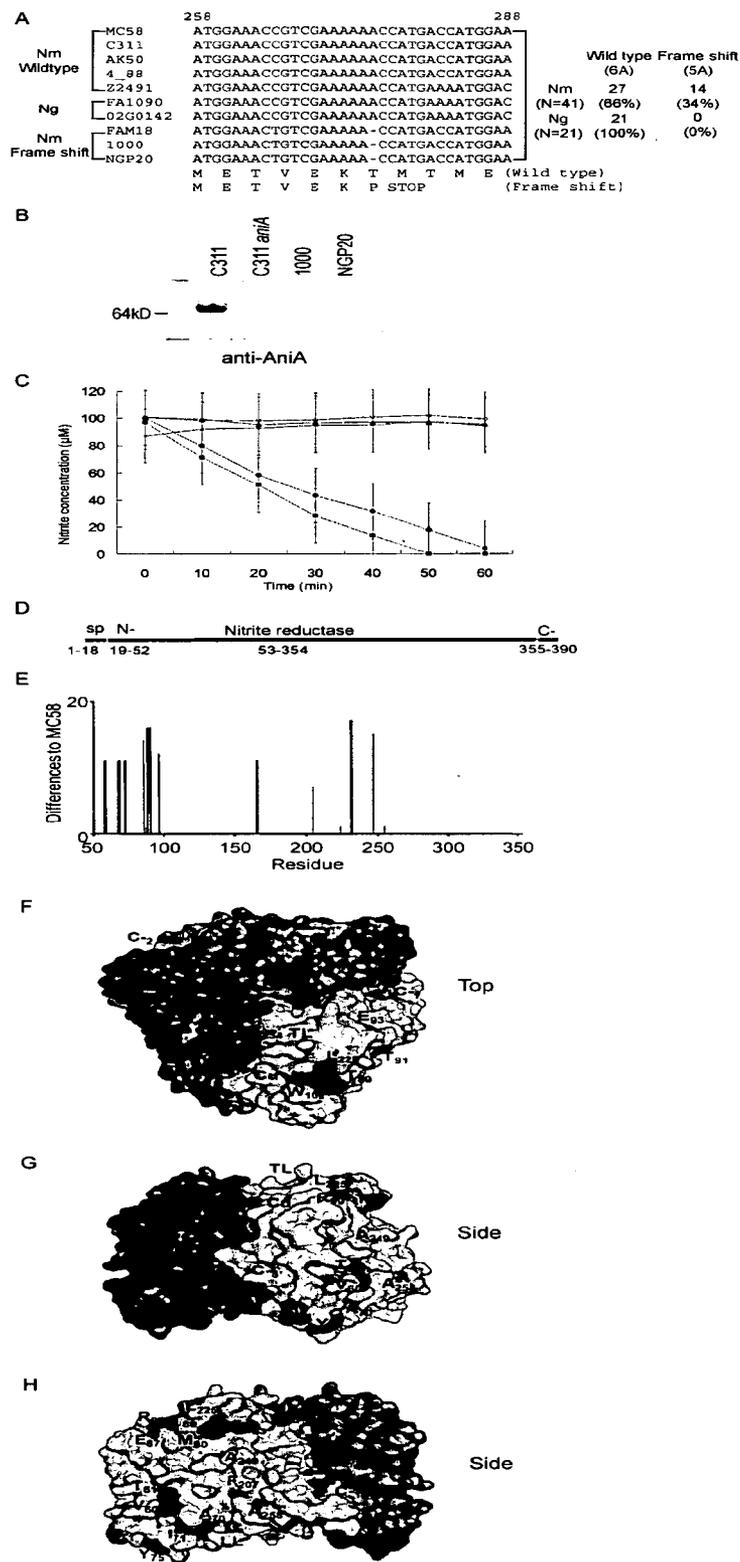


FIG. 4

FIG. 5A

MC58	ASLFAAACC	GEPAQAPAE	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE	100
C311	ASLFAAACC	GEPAQAPAL	FAAALAA	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
4758	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
AK50	ASLFAAACC	GEPAQAPAF	FAAAFAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B283	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
EG327	ASLFAAACC	GEPAQAPAE	FAAAFAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
RG329	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
NG3B24	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
NG144782	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B2169	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
44776	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
K2491	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
107	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
3758	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B2133	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
528	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
F3m18	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
10C0	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
NG320	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
425	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B6116/77	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
2970	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
DK353	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B210	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B2157	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B2163	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
MPJ31B	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
MPJ1E	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
MPJ8B	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
AK22	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
H33	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
H15	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
H36	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
40C	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B247	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
931905	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
88/034-5	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
MC/94	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
351	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
B2198	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE
MPJ3E	ASLFAAACC	GEPAQAPAE	FAAAEAAS	SAA	QTA	ETP	SSEL	DAV	THA	PEV	PPAI	DRD	YPA	KVR	KME	VE	KIM	KDD	GVE

FIG. 5B

MC58	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
C311	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
4783	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
AK50	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
B283	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
EG327	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
EG329	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
NGF324	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
NG144/82	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
B2169	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
44/76	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
Z249	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
107	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
3/83	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
B2133	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
528	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
Fam18	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
1000	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
NGE20	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
42B	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
D6116/77	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
2970	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
DK353	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
B2210	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
D2157	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
D2163	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
MPJ31D	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
MPJ11D	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
MPJ3B	ASL-FALAAACG	GFPAQAQPAE	TPAASAEAAAS	SAA-QTAA	ETPSGELPVI	DAVITHAPEV	PPAIDRDYPA	KVRVKMETVE	KTKKMDGVE
AK22	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
1115	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
1136	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
400	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
B247	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
931905	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
88/03415	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
M40/94	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
351	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
B2198	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE
MPJ3B	ASV-FALAAACG	EQAAK-PAE	TPAATASAEA	PAASNSQAAA	ETPSSELPVI	DAIVTHAPEV	PPPTDRDHEA	KVRVKMETVE	KTKKMDGVE

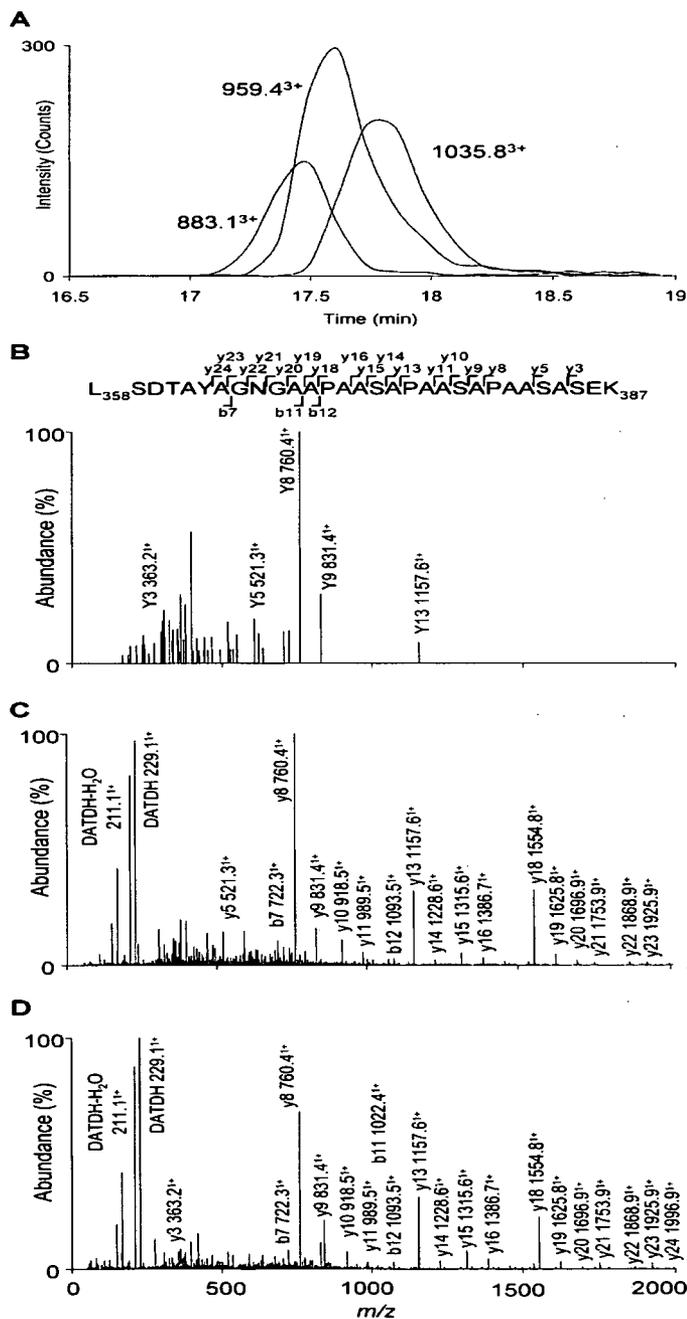


FIG. 6

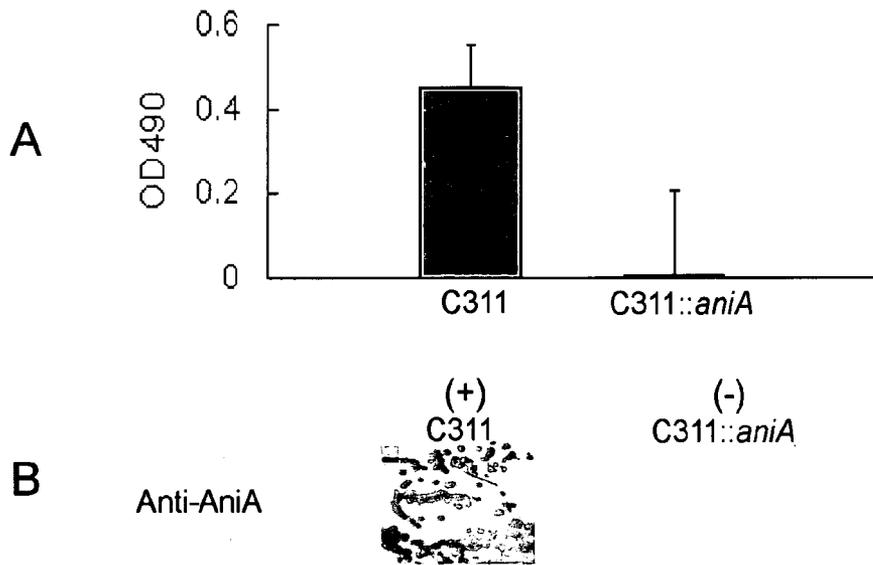


FIG. 7

SEQ ID NO: 1

MKRQALAAMIASLFALAACGGEPAAQAPAETPAAAAEAASSAAQTAAETPSGELPVIDAVTT
HAPEVPPAIDRDYPAKVRVKMETVEKTMEDGVEYRYWTFDGDVPGRMIRVREGDTVEVEF
SNNPSSTVPHNVDFHAATGQGGGAAATFTAPGRTSTFSFKALQPGLYIYHCAVAPVGMHIAN
GMYGLILVEPKEGLPKVDKEFYIVQGDFYTKGKKGAQGLQPFDMDKAVAEQPEYVVFNGHVG
AIAGDNALKAKAGETVRMYVGNGGPNLVSSFHVIGEIFDKVYVEGGKLINENVQSTIVPAGG
SAIVEFKVDIPGSYTLVDHSIFRAFNKGALGQLKVEGAENPEIM**DYKDDDDK**

FIG. 8

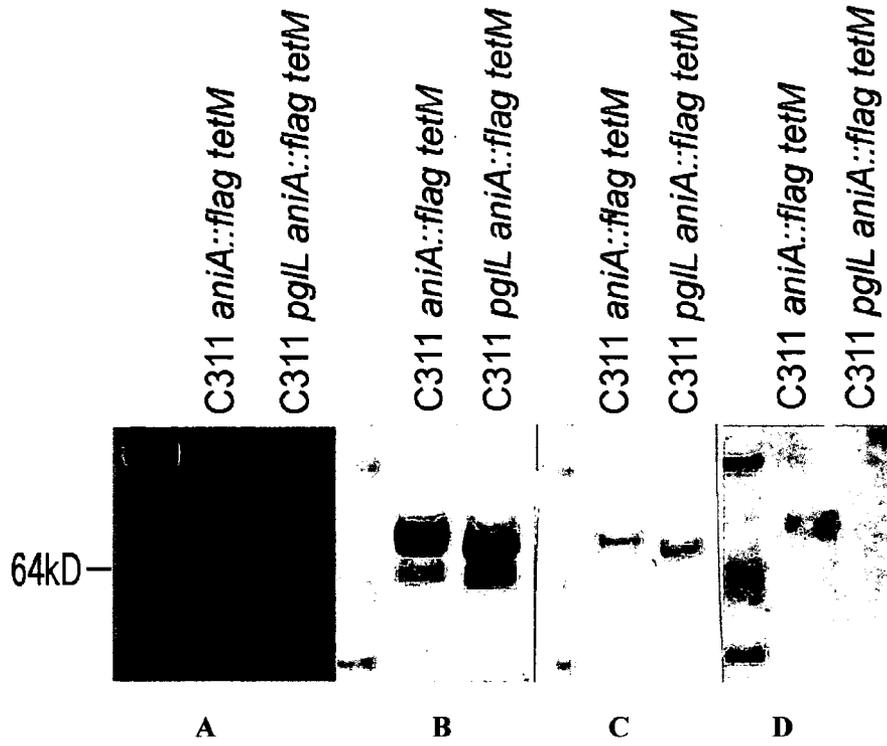


FIG. 9

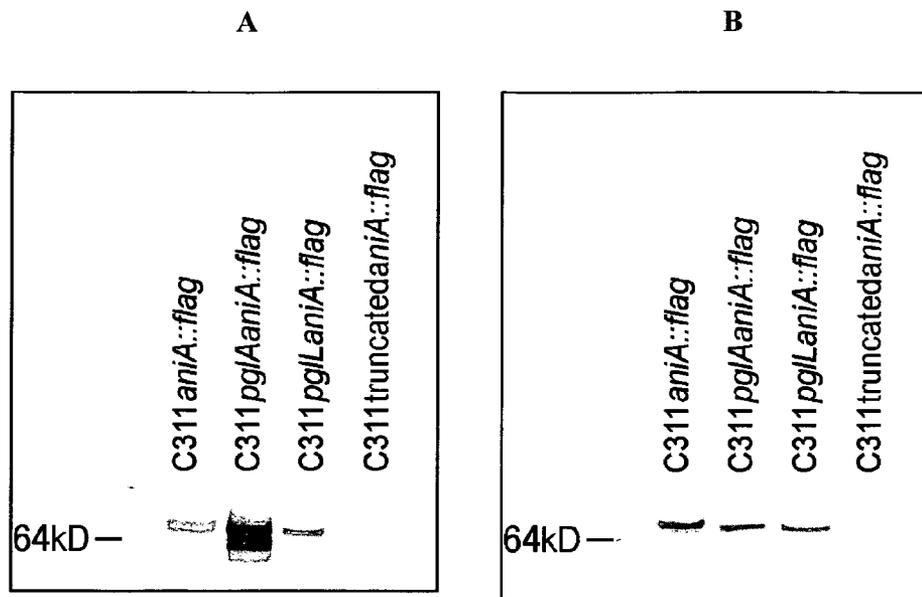


FIG. 10

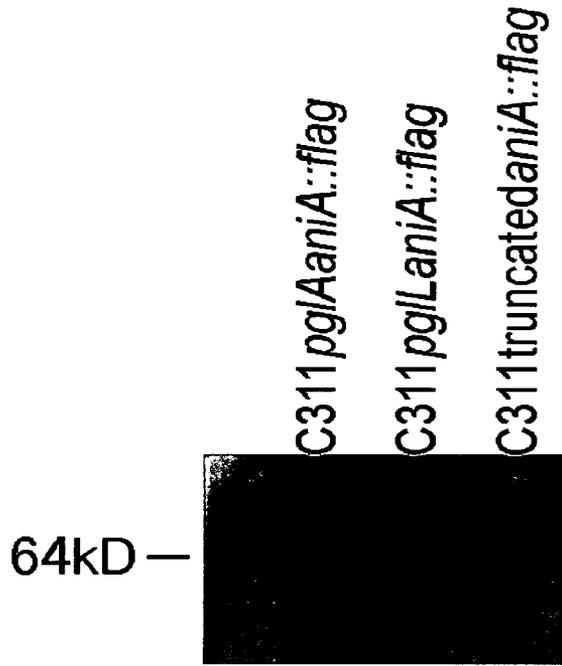


FIG. 11

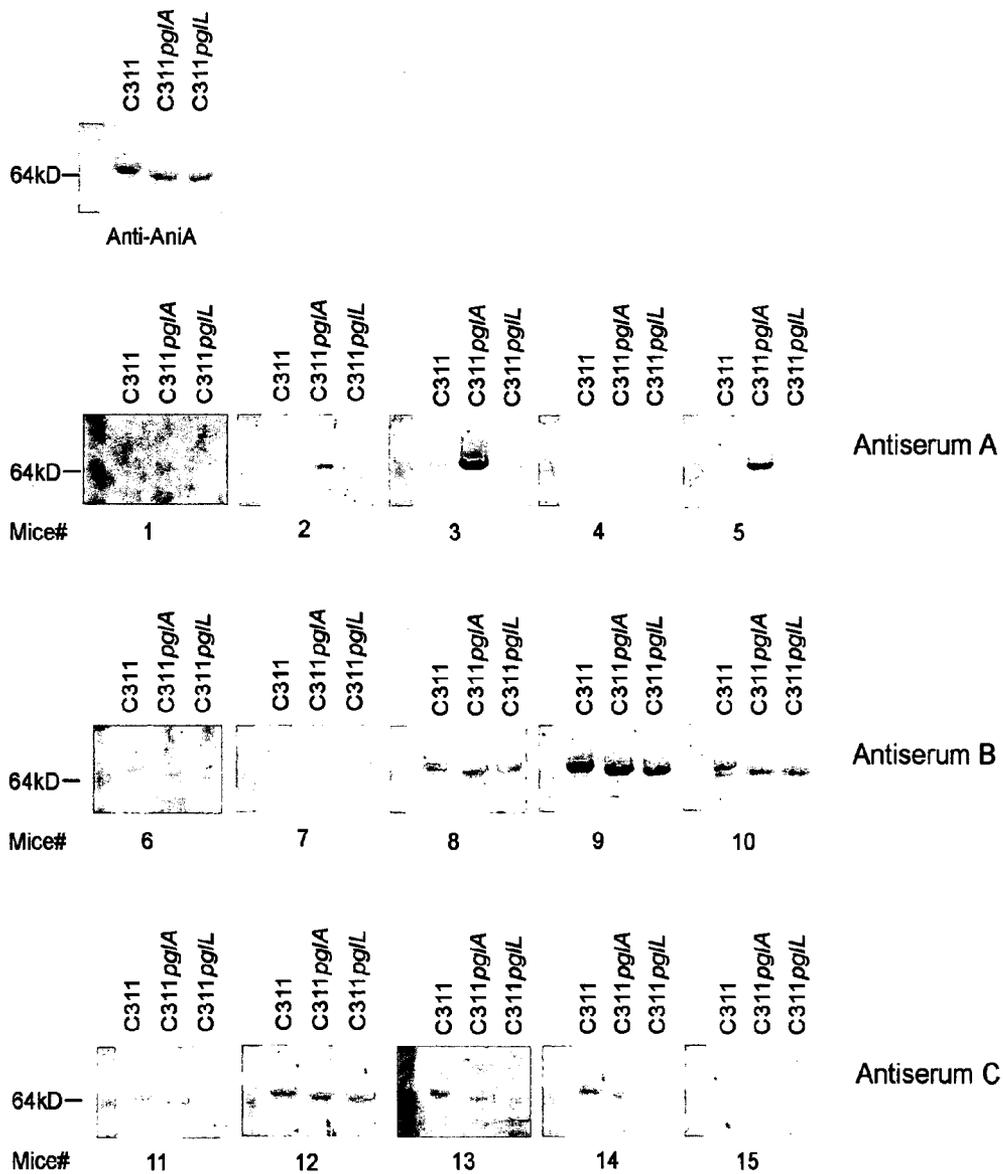


FIG. 12

SEQ ID NO: 2

Tc AniA#1

GSHMAAQATAETPAGELPVIDAVTTHAPEVPPAIDRDYPAKVRVKMETVEKTMKMDD
GVEYRYWTFDGDVPGRMIRVREGDTVEVEFSNNPSSTVPHNVDFHAATGQGGGAAAT
FTAPGRTSTFSFKALQPGLYIYHCAVAPVGMHIANGMYGLILVEPKEGLPKVDKEYF
IVQGDFYTKGKKGAQGLQPFDMDKAVAEQPEYVVFNGHVGA IAGDNALKAKAGETVR
MYVGNNGGPNLVSSFHVIGE I FDKVYVEGGK LINENVQSTIVPAGGSAIVEFKVDIPG
NYTLVDHSI FRAFNKGALGQLKVE

SEQ ID NO: 3

Tc AniA #2

GSHMAAQATAETPAGELPVIDAVTTHAPEVPPAIDRDYPAKVRVKMETVEKTMKMDD
GVEYRYWTFDGDVPGRMIRVREGDTVEVEFSNNPSSTVPHNVDFHAATGQGGGAAAT
FTAPGRTSTFSFKALQPGLYIYHCAVAPVGMHIANGMYGLILVEPKEGLPKVDKEYF
IVQGDFYTKGKKGAQGLQPFDMDKAVAEQPEYVVFNGHVGA IAGDNALKAKAGETVR
MYVGNNGGPNLVSSFHVIGE I FDKVYVEGGK LINENVQSTIVPAGGSAIVEFKVDIPG
NYTLVDHSI FRAFNKGALGQLKVEGAENPEIM

SEQ ID NO: 4

Tc AniA #3

GSHMAAQATAETPAGELPVIDAVTTHAPEVPPAIDRDYPAKVRVKMETVEKTMKMDD
GVEYRYWTFDGDVPGRMIRVREGDTVEVEFSNNPSSTVPHNVDFHAATGQGGGAAAT
FTAPGRTSTFSFKALQPGLYIYHCAVAPVGMHIANGMYGLILVEPKEGLPKVDKEYF
IVQGDFYTKGKKGAQGLQPFDMDKAVAEQPEYVVFNGHVGA IAGDNALKAKAGETVR
MYVGNNGGPNLVSSFHVIGE I FDKVYVEGGK LINENVQSTIVPAGGSAIVEFKVDIPG
NYTLVDHSI FRAFNKGALGQLKVEGAENPEIMTQKLSDTAYAGSG

SEQ ID NO: 5

Tc AniA#4

GSHMAAQATAETPAGELPVIDAVTTHAPEVPPAIDRDYPAKVRVKMETVEKTMKMDD
GVEYRYWTFDGDVPGRMIRVREGDTVEVEFSNNPSSTVPHNVDFHAATGQGGGAAAT
FTAPGRTSTFSFKALQPGLYIYHCAVAPVGMHIANGMYGLILVEPKEGLPKVDKEYF
IVQGDFYTKGKKGAQGLQPFDMDKAVAEQPEYVVFNGHVGA IAGDNALKAKAGETVR
MYVGNNGGPNLVSSFHVIGE I FDKVYVEGGK LINENVQSTIVPAGGSAIVEFKVDIPG
NYTLVDHSI FRAFNKGALGQLKVEGAENPEIMTQKLSDTAYAGSGAASAPAA
SAPAASASEKSVY

SEQ ID NO: 6

Tc AniA#5

GSHMELPVIDAVTTHAPEVPPAIDRDYPAKVRVKMETVEKTMKMDDGVEYRYWTFDG
DVPGRMIRVREGDTVEVEFSNNPSSTVPHNVDFHAATGQGGGAAATFTAPGRTSTFS
FKALQPGLYIYHCAVAPVGMHIANGMYGLILVEPKEGLPKVDKEYFIVQGDFYTKGK
KGAQGLQPFDMDKAVAEQPEYVVFNGHVGA IAGDNALKAKAGETVRMYVGNNGGPNLV
SSFHVIGE I FDKVYVEGGK LINENVQSTIVPAGGSAIVEFKVDIPGNYTLVDHSI FR
AFNKGALGQLKVE

FIG. 13

SEQ ID NO: 7

Tc AniA #6

GSHMELPVIDAVTTHAPEVPPAIDRDYPAKVRVKMETVEKTMKMDGVEYRYWTFDG
DVPGRMIRVREGDTVEVEFSNNPSSTVPHNVDFHAATGQGGGAAATFTAPGRTSTFS
FKALQPGLYIYHCAVAPVGMHIANGMYGLILVEPKEGLPKVDKEFYIVQGDFYTKGK
KGAQGLQPFDMDKAVAEQPEYVVFNGHVGA IAGDNALKAKAGETVRMYVGNGGPNLV
SSFHVIGEIFDKVYVEGGKLINENVQSTIVPAGGSAIVEFKVDIPGNYTLVDHSIFR
AFNKGALGQLKVEGAENPEIM

SEQ ID NO: 8

Tc AniA #7

GSHMELPVIDAVTTHAPEVPPAIDRDYPAKVRVKMETVEKTMKMDGVEYRYWTFDG
DVPGRMIRVREGDTVEVEFSNNPSSTVPHNVDFHAATGQGGGAAATFTAPGRTSTFS
FKALQPGLYIYHCAVAPVGMHIANGMYGLILVEPKEGLPKVDKEFYIVQGDFYTKGK
KGAQGLQPFDMDKAVAEQPEYVVFNGHVGA IAGDNALKAKAGETVRMYVGNGGPNLV
SSFHVIGEIFDKVYVEGGKLINENVQSTIVPAGGSAIVEFKVDIPGNYTLVDHSIFR
AFNKGALGQLKVEGAENPEIMTQKLSDTAYAGSG

SEQ ID NO: 9

Tc AniA #8

GSHMELPVIDAVTTHAPEVPPAIDRDYPAKVRVKMETVEKTMKMDGVEYRYWTFDG
DVPGRMIRVREGDTVEVEFSNNPSSTVPHNVDFHAATGQGGGAAATFTAPGRTSTFS
FKALQPGLYIYHCAVAPVGMHIANGMYGLILVEPKEGLPKVDKEFYIVQGDFYTKGK
KGAQGLQPFDMDKAVAEQPEYVVFNGHVGA IAGDNALKAKAGETVRMYVGNGGPNLV
SSFHVIGEIFDKVYVEGGKLINENVQSTIVPAGGSAIVEFKVDIPGNYTLVDHSIFR
AFNKGALGQLKVEGAENPEIMTQKLSDTAYAGSGAASAPAASAPAASAPAASASEKS
VY

FIG. 13, continued

MUTANT BACTERIAL GLYCOPROTEINS AND USES THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

This is the U.S. National Stage of International Application No. PCT/AU2009/001111, filed Aug. 28, 2009 which was published in English under PCT Article 21(2), which in turn claims the benefit of Australia Patent Application No. 2008904429, filed Aug. 28, 2008, and which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

THIS INVENTION relates to mutant glycoproteins of pathogenic bacteria, such as *Neisseria*, lacking one or more post-translational modifications and their use in immunotherapy and/or vaccines.

BACKGROUND OF THE INVENTION

Disease caused by Group B *Neisseria meningitidis* (*N. meningitidis*) remains a significant health problem worldwide. There are currently no effective vaccines available for this Group, although effective treatment for meningococcal infections is available with antibiotics. However, the progression of the infection can be so rapid that in some cases treatment cannot be administered in time to be effective. The threat of meningococcal disease would be most appropriately dealt with by prevention with a generally effective vaccine. There is also no vaccine to prevent infection by the related pathogen *Neisseria gonorrhoea* (*N. gonorrhoeae*). Although effective treatment of gonococcal infections is currently available with antibiotics, resistance is increasing. Furthermore, in gonococcal infections, asymptomatic carriage (particularly common in women) can result in greater susceptibility to HIV, and may also lead to pelvic inflammatory disease.

Pili of pathogenic *Neisseria* are typical of a family of adhesins, type IV fimbriae, found in a wide range of Gram-negative pathogens. These long polymeric proteins protrude from the bacterial surface and have a crucial role in both colonization of the host and adhesion to host cells (Virji et al., 1991; McGee & Stephens, 1984). Although there are other accessory proteins, pili are composed primarily of thousands of subunits, called pilin. Pili of pathogenic *Neisseria* are major virulence factors associated with adhesion, cytotoxicity, twitching motility, auto-aggregation and DNA transformation.

Typical of many surface proteins of pathogenic *Neisseria*, pili display both phase and antigenic variation (reviewed in Seifert, 1996) and are post-translationally modified (reviewed in Virji, 1997). Four different types of modifications have been described. A phosphodiester-linked glycerol substituent has been reported at serine 93 of the pilin molecule (Stimson et al., 1996), a phosphate group has been reported at serine 68 in *N. gonorrhoeae* (Forest et al., 1999), pili of both *N. meningitidis* and *N. gonorrhoeae* are glycosylated at serine 623 with a trisaccharide molecule, Gal (β 1-4) Gal (α 1-3) 2,4-diacetimidido-2,4,6-trideoxyhexose (Stimson et al., 1995) or a disaccharide Gal (α 1-3) GlcNAc (Parge et al., 1995; Marceau et al., 1998). Covalently linked phosphorylcholine (ChoP) has been reported in *N. meningitidis* and *N. gonorrhoeae* (Kolberg et al., 1997; Weiser et al., 1998) and is found on surface-exposed moieties of many different pathogens of the respiratory tract (Gillespie et al., 1996 J Med Microbiol

44:35-40). In *H. influenzae*, *S. pneumoniae* and commensal *Neisseria*, ChoP is attached to lipopolysaccharide (LPS) and the biosynthetic pathway is well understood (Serino and Virji, 2000 Microbiology 35:1550; Weiser et al., 1989 57:3045-52; Zhang et al., 1999 Mol Microbiol 31:1477)

However, in pathogenic *Neisseria*, ChoP is covalently attached to the surface exposed pili but is not found attached to the LPS (Weiser et al., 1998 Infection & Immunity 66:4263). The position of the ChoP modification has been determined in *N. gonorrhoeae* at Serine 68 in strain MS11 (Aas et al., 2006 Journal of Biological Chemistry. 281:27712-27723). The transferase required for the ChoP to pilin of *N. meningitidis*, pptA, has been identified previously (Warren and Jennings, 2003 Infection and Immunity 71:6892-68928).

The same gene was subsequently identified in *N. gonorrhoeae* (Hegge et al., 2004 Proc Natl Acad Sci USA 101: 10798-10803).

The role of phosphorylcholine in disease caused by pathogenic *Neisseria* is not known, nor has the function of pili post-translational modifications in host-pathogen interactions been resolved.

SUMMARY OF THE INVENTION

The present invention relates to the use of mutant glycoproteins from pathogenic bacteria lacking one or more ChoP and/or glycosylation post-translational modifications, or having modified glycosylation, as immunogens.

More particularly, the present invention relates to the surprising discovery that removal of "masking" structures from *Neisseria* glycoproteins, such as sugars and/or ChoP, can alter the proteins such that they elicit a "non-native" immune response, preferably protective against subsequent infection by the bacterium.

In a first aspect, the invention provides an isolated mutant protein of a bacterial pathogen, said isolated mutant protein lacking one or more phosphorylcholine, glycosylation and/or other post-translational modifications, or having modified glycosylation, compared to a corresponding wild-type protein thereof, including homologues or fragments thereof.

Suitably, said isolated mutant protein, or fragment thereof, is capable of eliciting an altered immune response in a host compared to a corresponding wild-type glycoprotein.

In one embodiment, said isolated mutant protein is a mutant pilin protein.

In another embodiment, said isolated mutant protein, or fragment thereof, is a mutant nitrite reductase.

Typically, said isolated mutant protein comprises an amino acid substitution or deletion that removes glycosylation.

In one particular embodiment, the bacterial pathogen is of a genus of *Neisseria*.

Preferably, said bacterial pathogen is of a species of *Neisseria meningitidis* or *Neisseria gonorrhoeae*.

In a preferred embodiment, the mutant protein is a mutant nitrite reductase.

In particular embodiments, the isolated mutant protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-9.

In a second aspect, the invention provides an isolated nucleic acid encoding (i) the isolated mutant protein of the first aspect, wherein said isolated mutant protein comprises an amino acid substitution or deletion that removes glycosylation, or (ii) a fragment of the isolated mutant protein of the first aspect.

In a third aspect, the invention provides an expression construct comprising the isolated nucleic acid of the second aspect, operably linked to one or more regulatory nucleotide sequences.

In a fourth aspect, the invention provides a bacterial cell comprising isolated mutant protein, or fragment thereof, of the first aspect.

In one embodiment, the bacterial cell is a host cell comprising the expression construct of the third aspect.

In another embodiment, the bacterial cell is produced by mutagenesis to thereby remove, inhibit or modify glycosylation of a bacterial glycoprotein.

Suitably, said bacterial cell is of a genus of *Neisseria* or is *E. coli*.

In a fifth aspect, the invention provides a method of producing the isolated mutant protein of the first aspect, or fragment thereof, in recombinant form, said method including the step of expressing said isolated mutant protein, or fragment thereof, in the bacterial host cell of the fourth aspect.

In a sixth aspect, the invention provides an antibody which binds, or is raised against, (i) the isolated mutant protein of the first aspect, or a fragment thereof, or (ii) the isolated mutant protein, or fragment thereof, produced according to the fifth aspect.

In a seventh aspect, the invention provides an immunogenic composition comprising (i) one or more one or more of the isolated mutant proteins of the first aspect, or a fragment thereof, (ii) the bacterial host cell of the fourth aspect; (iii) the isolated mutant protein, or fragment thereof, produced according to the method of the fifth aspect, and/or (iv) the antibody of the sixth aspect, and a carrier, diluent or excipient.

In an eighth aspect, the invention provides a method of eliciting an immune response in a host, said method including the step of administering to said host (i) one or more one or more of the isolated mutant proteins of the first aspect, or a fragment thereof, (ii) the bacterial host cell of the fourth aspect; (iii) the isolated mutant protein, or fragment thereof, produced according to the method of the fifth aspect, and/or (iv) the antibody of the sixth aspect, to thereby elicit an immune response in said host.

In a ninth aspect, the invention provides use of an agent selected from the group consisting of: (i) one or more one or more of the isolated mutant proteins of the first aspect, or a fragment thereof, (ii) the bacterial host cell of the fourth aspect; (iii) the isolated mutant protein, or fragment thereof, produced according to the method of the fifth aspect, and/or (iv) the antibody of the sixth aspect, for prophylactically or therapeutically treating a disease or condition caused by a bacterial pathogen in a host.

The host may be any animal, inclusive of mammals such as domestic animals, livestock, performance animals and humans.

Preferably, the host is a human.

Throughout this specification, unless otherwise indicated, "comprise", "comprises" and "comprising" are used inclusively rather than exclusively, so that a stated integer or group of integers may include one or more other non-stated integers or groups of integers.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 Coomassie stain and western analysis of Flag-tagged pilin antigen for mouse immunization. Flag-tagged pilin antigens purified from C311 wild type, C311pglA, C311pptA, C31126ApglA were loaded on 4-12% Bis-Tris Novex gel and analysis by coomassie stain and western blots with anti-Flag mAb.

FIG. 2 Monitor of immune response by western blots analysis of vortex pilin probing with mouse antisera raised against pilin-WT, pilin-pglA, pilin-pptA and pilin-26ApglA.

FIG. 3 Identification of AniA as a glycoprotein in *N. meningitidis* and *N. gonorrhoeae* by SDS-PAGE and Western blot analysis. (A-D) Analysis of Outer membrane Proteins (OMPs) of *N. meningitidis* C311 and mutant strains C311pilE, C311pglA, C311porA, C311frpB and C311aniA on Western blot. Glycoproteins with addition of trisaccharides were revealed by the use of polyclonal antibody anti-trisaccharide. (E) Analysis of C311 and C311aniA by Western blot against monoclonal antibody AniA. (F) Western blot analysis of the migration of AniA isolated from *N. meningitidis* strain C311, and glycosylation pathway mutant strains C311pglE, C311pglA and C311pglB, and (G) *N. gonorrhoeae* strain 1291, glycosylation pathway mutant strains 1291pglA and 1291pglD. AniA was identified by the use of a monoclonal antibody "anti-AniA". (H) Analysis of 1291 and 1291aniA by Western blot against monoclonal antibody anti-AniA.

FIG. 4A is a nucleotide sequence alignment of aniA of *N. meningitidis* and *N. gonorrhoeae* strains, compared with the aniA sequence of *N. meningitidis* strain MC58 aniA sequence from base pairs 258-288 (Swiss-prot entry Q9JYE1). To the right of the comparison is the result of a survey of the frame shift mutation (6 adenosine (6A) or 5 adenosine (5A) allele) in 42 *N. meningitidis* (data derived from FIG. 5A) and 21 *N. gonorrhoeae* strains (Power, et al., 2007 Infection and Immunity 75: 3202). FIG. 4B is an image of Western analysis of *N. meningitidis* strain C311, C311aniA and "frame shift" strains 1000 and NGP20 with anti-AniA. FIG. 4C is a graph showing nitrite utilization vs time for wild-type C311 (filled circles), C311pglA (filled squares), C311aniA (filled triangles), and *N. meningitidis* frame shift strains 1000 (cross) and NGP20 (open circles). The cultures were supplemented with 100 μ M nitrite, culture samples were collected every 10 minutes for 1 hour and the utilization of nitrite was measured colourimetrically (Anjum et al., 2002 J. Bacteriol, 184: 2087). Results are the mean of triplicate independent biological samples. Error bars show ± 1 standard deviation. FIGS. 4D and 4E are diagrams showing variation in amino acid for each residue of *N. meningitidis* AniA sequenced from 41 clinical isolates aligned against *N. meningitidis* strain MC58 AniA (see also FIGS. 5A and B). In FIG. 4D, the bar represents the full length AniA protein; sp, cleaved signal peptide with palmitoylated cysteine (1-18); N—, N-terminal repeat region (19-52); Nitrite reductase, core protein (53-354); C—, glycosylated C-terminal repeat region. NB. The region of the protein expressed and purified to determine the 3D structure of AniA "core protein" from *N. gonorrhoeae* is shown as a black line (RCSB Protein Data Bank accession 1KVS) FIG. 4E shows the number of differences seen at each amino acid position in the comparison of AniA from *N. meningitidis* strain MC58 and 42 *N. meningitidis* strains. Differences are plotted on the Y-axis. The plot only shows the differences over the region covered by the AniA "core protein" (53-354), and was used to determine the sites of highest amino acid sequence variation in the 3D structure. Black lines report differences in comparison of wild type, full length proteins (see FIG. 5A alignment), orange lines report additional differences seen when examining theoretical translations of "frame shift" strains (FIG. 5B). FIGS. 4F-H are representations of MC58 AniA "core protein" trimer modelled on AniA of *N. gonorrhoeae* (RCSB Protein Data Bank accession 1KVS). Each monomer is shown in a different shade of grey. Residues of interest are only coloured in one monomer (light grey). Top view (FIG. 4F); side view (FIG. 4G), rotated 90° from FIG. 4F; and side view (FIG. 4H),

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rotated 90° from FIG. 4G. Red, variable amino acids in sequenced wild type *N. meningitidis* clinical isolates; green N_{-1,2,3}, N-terminal modelled residue, end of variable N-terminal repeat region; cyan C_{-1,2,3}, C-terminal modelled residue, start of glycosylated C-terminal repeat region; yellow Cu, Copper centre (buried); pale green TL and LL, Tower loop and Linker loop (deleted regions in Neisserial AniA); blue, proposed surface electron transport routes.

FIG. 5 AniA amino acid sequence alignment of 41 *N. meningitidis*. (A) AniA amino acid sequence alignment of 41 *N. meningitidis* strains, including 9 strains with full length sequences and 32 strains with sequences from position 11-349. SEQ ID NOS are as follows: MC58=SEQ ID NO: 31; C311=SEQ ID NO: 32; 4/88=SEQ ID NO: 33; AK50=SEQ ID NO: 34; BZ 83=SEQ ID NO: 35; EG327=SEQ ID NO: 36; EG329=SEQ ID NO: 37; NGPB24=SEQ ID NO: 38; NG144/82=SEQ ID NO: 39; BZ 169=SEQ ID NO: 40; 44/76=SEQ ID NO: 41; Z2491=SEQ ID NO: 42; 107=SEQ ID NO: 43; 3/88=SEQ ID NO: 44; BZ133=SEQ ID NO: 45; 528=SEQ ID NO: 46; FAM18=SEQ ID NO: 47; 1000=SEQ ID NO: 48; NGP20=SEQ ID NO: 49; 42B=SEQ ID NO: 50; B6116/77=SEQ ID NO: 51; 2970=SEQ ID NO: 52; DK353=SEQ ID NO: 53; BZ210=SEQ ID NO: 54; BZ157=SEQ ID NO: 55; BZ163=SEQ ID NO: 56; MPJ31B=SEQ ID NO: 57; MPJ1B=SEQ ID NO: 58; MPJ8B=SEQ ID NO: 59; AK22=SEQ ID NO: 60; H38=SEQ ID NO: 61; H15=SEQ ID NO: 62; H36=SEQ ID NO: 63; 400=SEQ ID NO: 64; BZ47=SEQ ID NO: 65; 931905=SEQ ID NO: 66; 88/03415=SEQ ID NO: 67; M40/94=SEQ ID NO: 68; 351=SEQ ID NO: 69; BZ198=SEQ ID NO: 70; MPJ3B=SEQ ID NO: 71. (B) AniA amino acid sequence alignment of wild-type AniA strains and theoretical translations of "frame shift" strains. Shaded residues showed variation within the strains analysed. SEQ ID NOS are as follows: MC58=SEQ ID NO: 72; C311=SEQ ID NO: 73; 4/88=SEQ ID NO: 74; AK50=SEQ ID NO: 75; BZ 83=SEQ ID NO: 76; EG327=SEQ ID NO: 77; EG329=SEQ ID NO: 78; NGPB24=SEQ ID NO: 79; NG144/82=SEQ ID NO: 80; BZ 169=SEQ ID NO: 81; 44/76=SEQ ID NO: 82; Z2491=SEQ ID NO: 83; 107=SEQ ID NO: 84; 3/88=SEQ ID NO: 85; BZ133=SEQ ID NO: 86; 528=SEQ ID NO: 87; FAM18=SEQ ID NO: 88; 1000=SEQ ID NO: 89; NGP20=SEQ ID NO: 90; 42B=SEQ ID NO: 91; B6116/77=SEQ ID NO: 92; 2970=SEQ ID NO: 93; DK353=SEQ ID NO: 94; BZ210=SEQ ID NO: 95; BZ157=SEQ ID NO: 96; BZ163=SEQ ID NO: 97; MPJ31B=SEQ ID NO: 98; MPJ1B=SEQ ID NO: 99; MPJ8B=SEQ ID NO: 100; AK22=SEQ ID NO: 101; H38=SEQ ID NO: 102; H15=SEQ ID NO: 103; H36=SEQ ID NO: 104; 400=SEQ ID NO: 105; BZ47=SEQ ID NO: 106; 931905=SEQ ID NO: 107; 88/03415=SEQ ID NO: 108; M40/94=SEQ ID NO: 109; 351=SEQ ID NO: 110; BZ198=SEQ ID NO: 111; MPJ3B=SEQ ID NO: 112.

FIG. 6 Tryptic peptides and glycopeptides from flag tagged AniA purified from *N. meningitidis* strain C311pglA cells analysed by LC-ESI-MS/MS. FIG. 6A shows extracted ion chromatograms of ions corresponding to the tryptic peptide L₃₅₈-K₃₈₇ (with N₆₆ deamidated) and the same peptide with one or two DATDH monosaccharides (triple charged ions at m/z of 883.1, 959.4 and 1035.8 respectively). FIGS. 6B-6D show MS/MS spectra of non-glycosylated (FIG. 6B), mono-glycosylated (FIG. 6C), and di-glycosylated (FIG. 6D) L₃₅₈-K₃₈₇ tryptic peptide.

FIG. 7 Analysis of the surface expression of AniA by whole cell ELISA and immuno-colony blot. (A) Whole cell ELISA on AniA from wild-type C311 (blue) and mutant C311aniA (red) by the use of monoclonal antibody anti-AniA. The

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results are the mean of triplicates. Error bar indicates ±1 standard deviation from the mean. (B) Immuno-colony blot against monoclonal antibody anti-AniA from wild-type C311 (left) and mutant C311aniA (right).

FIG. 8 Amino acid sequence of truncated FLAG-tagged AniA from *N. meningitidis* strain C311 (SEQ ID NO:1). As described in Example 5. Flag peptide is shown in bold.

FIG. 9 Western blot analysis of AniA-FLAG. AniA-FLAG purified from wild type C311 and C311pglL were loaded on 4-12% Bis-tris Novex gel and analysed by (A) commassie staining and (B) Western blots with anti-FLAG, (C) anti-AniA mAb and (D) anti-trisaccharide sera.

FIG. 10 Analysis of immune response by Western blot analysis of purified truncated AniA-FLAG. AniA-FLAG purified from wild type C311, C311pglA and C311pglL were loaded on 4-12% Bis-tris Novex gel and analysed by (A) Western blots with polyclonal rabbit anti-AniA anti-sera and (B) anti-AniA monoclonal antibody.

FIG. 11 Western blot analysis of AniA-FLAG antigen for immunisation of mice. AniA-FLAG purified from wild type C311, C311pglA and C311pglL were loaded on 4-12% Bis-tris Novex gel and analysed by Western blot with anti-AniA mAb.

FIG. 12 Western blot analysis immune response against outer membrane proteins preparations from C311, C311pglA and C311pglL using mouse antisera raised against purified flag tagged antigens; (A) AniA-PglA, (B) truncated AniA and (C) AniA-PglL.

FIG. 13 Truncated AniA proteins amplified from *N. gonorrhoeae* strain 1291 for expression in *E. coli*.

BRIEF DESCRIPTION OF THE SEQUENCE LISTING

The Sequence Listing is submitted as an ASCII text file named Sequence_Listing.txt, which was created on Jun. 19, 2011, and is 246,223 bytes, which is incorporated by reference herein.

SEQ ID NO: 1: Truncated FLAG-tagged AniA (FIG. 8).

SEQ ID NOS: 2-9: Truncated AniA proteins amplified from *N. gonorrhoeae* strain 1291 for expression in *E. coli* (FIG. 13).

SEQ ID Nos: 10-14: Primer sequences (Table 1).

SEQ ID Nos: 15-20: Primer sequences (Table 2).

SEQ ID Nos: 21-30: Nucleotide sequence alignment of AniA of *N. meningitidis* and *N. gonorrhoeae* strains, compared with the AniA of *N. meningitidis* strain MC58 AniA sequence from base pairs 258-288 (FIG. 4A).

SEQ ID Nos: 31-71: AniA amino acid sequence alignment of 41 *N. meningitidis* strains, including 9 strains with full length sequences and 32 strains with sequences from positions 11-349 (FIG. 5A).

SEQ ID Nos: 72-112: AniA amino acid sequence alignment of wild-type AniA strains and theoretical translations of "frame shift" strains (FIG. 5B).

DETAILED DESCRIPTION OF THE INVENTION

The present invention is relates to mutant, modified or otherwise altered forms of bacterial glycoproteins such as pilin and nitrite reductase, particularly from pathogenic bacteria such as but not limited to *Neisseria*, and their use as immunogens. In preferred forms, the invention provides a mutant pilin protein lacking one or more of ChoP and glycosylation and/or a mutant nitrite reductase protein that lacks, or has modified, glycosylation. Pilin proteins are normally present on the bacterial surface and have a crucial role in both

colonization of the host and adhesion to host cells. Wild-type pilin of pathogenic *Neisseria* contains both ChoP and glycosylation post-translational modifications. The invention also relates to another glycoprotein of *Neisseria*, AniA, which is an anaerobically induced nitrite reductase that is glycosylated by the same pathway. This demonstrates that the pilin glycosylation pathway is a general pathway for O-glycosylation in *Neisseria*. Unlike pilin, the AniA glycoprotein is not covalently modified by ChoP. It is therefore proposed that wild-type pilin and wild-type nitrite reductase thus contribute to human host-colonization.

It is also proposed that glycosylation, and/or Cho-P post-translational modification of certain bacterial proteins (including but not limited to pilin and nitrate reductase of *Neisseria* species) constitute "masking" structures that facilitate immune evasion by pathogenic bacteria. These masking structures may normally elicit a "native" immune response which is predominantly directed to the masking structure but which is not protective or otherwise useful to the host.

More particularly, the present invention is directed to the production and use of isolated pilin and nitrite reductase proteins, or fragments thereof, that lack "masking" structures such as tri-saccharide sugars and/or ChoP to thereby elicit an altered immune response which is more beneficial to the host.

By "altered" in this context is meant distinct, "non-native" immune response that preferably protects against subsequent infection by the bacterium, or is at least more immunologically effective than the native immune response. By removing either ChoP and/or sugar groups, or by reducing the number of the sugar groups from a bulky trisaccharide to a di- or monosaccharide group, the mutant pilin and/or nitrite reductase underlying conserved structure will be more exposed, or "unmasked" to thereby enable both novel and improved antigen processing and hence a more protective immune response.

Although the present invention is exemplified herein with respect to generating novel immune responses to bacterial pathogens of the genus *Neisseria*, such as *N. meningitidis* and *N. gonorrhoeae*, the general principle provided by the present invention is applicable to Gram-negative or Gram-positive bacterial pathogens with surface expressed post-translationally modified proteins. Furthermore, while the pilin and nitrite reductase glycoproteins exemplified herein comprise O-linked glycosylation, the invention may also be practised with N-linked glycoproteins.

Particular, non-limiting examples of other pathogenic bacteria include bacteria of the genera *Campylobacter*, *Helicobacter*, *Pseudomonas* and *Mycobacterium*. For example, reference is made to Wacker et al., 2002 Science 298 790 and Szymanski et al., 1999, Mol. Microbiol. 32 1022. Particular reference is also made to reviews by Power & Jennings, 2003, EMS Microbiol. Lett. 218 211 and Szymanski & Wren, 2005, Nat. Rev. Microbiol. 3 225, which describe several other bacterial glycoproteins that may be modified according to the present invention.

For the purposes of this invention, by "isolated" is meant material that has been removed from its natural state or otherwise been subjected to human manipulation. Isolated material may be substantially or essentially free from components that normally accompany it in its natural state, or may be manipulated so as to be in an artificial state together with components that normally accompany it in its natural state. Isolated material may be in native, chemical, synthetic or recombinant form.

By "antigenic" is meant capable of being recognized by components of the host immune system, such as antibodies.

By "immunogenic" is meant capable of eliciting an immune response, preferably a protective immune response upon administration to a host.

By "protein" is meant an amino acid polymer comprising D- or L-amino acids and/or natural or non-natural amino acids as are well understood in the art.

A "peptide" is a protein having no more than fifty (50) amino acids.

A "polypeptide" is a protein having more than fifty (50) amino acids.

Throughout this specification, a "glycoprotein" is a protein, peptide or polypeptide that comprises one or more glycosyl moieties or is otherwise "glycosylated" as is well known in the art. This definition includes O-linked and N-linked glycosylation. Preferably, the glycosyl moieties or glycosylation is O-linked to the protein via a serine or threonine residue. By way of example only, reference may be made to Chapter 12 of Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE (John Wiley & Sons Inc. NY, 1991-2008), which provides the skilled reader with general information about the structure, analysis and preparation of glycoproteins.

By "mutant" is meant a protein lacking one or more of ChoP, glycosylation and/or other post-translational modifications, or having modified glycosylation compared to a wild-type glycoprotein.

Such mutant proteins may have amino acid substitutions, additions and/or deletions (e.g truncations) that substantially or completely prevent or inhibit glycosylation and/or Cho-P addition.

By way of example, a pilin glycoprotein of *N. meningitidis* may be glycosylated at serine 63 or a corresponding S or T residue that is capable of O-linked glycosylation. Reference to serine 63 of *N. meningitidis* pilin is made herein in the context of the pilin sequence described in Power et al., 2006, supra and other pilin sequences such as available under Genbank accession nos: AAA25487 and AAA67333. It will also be appreciated that the invention also extends to homologous serine or threonine residues in pilin and other bacterial proteins that are capable of capable of O-linked glycosylation.

Cho-P modification of pilin may be at serine 68 in *N. gonorrhoeae* strain MS11 or serine 156 and/or 160 on pilin of *N. meningitidis* strain C311.

Also by way of example, a nitrite reductase protein may be O-glycosylated at one or more carboxy terminal serine-containing peptide repeats, or homologous sequences in nitrite reductase protein and other bacterial proteins that are capable of capable of O-linked glycosylation. In this regard, reference is made to FIG. 5, for guidance as to the location of carboxy terminal serine-containing peptide repeats of *N. meningitidis* AniA nitrite reductase in a variety of *N. meningitidis* strains.

In further embodiments, a mutant nitrite reductase protein may comprise N-terminal deletions in addition to deletion of one or more carboxy terminal serine-containing peptide repeats.

In certain embodiments, the mutant proteins comprise a substitution and/or deletion of one or more amino acids at these exemplary glycosylation sites.

Particular, non-limiting examples of embodiments of a nitrite reductase of *N. meningitidis* (SEQ ID NO: 1) or *N. gonorrhoeae* (SEQ ID NOs: 2-9) having deletions of an O-linked glycosylation site are provided.

In another embodiment, the mutant protein is produced in a genetically-modified bacterium to produce a mutant protein having modified glycosylation. Non-limiting examples of modified glycosylation include O-linked monosaccharides such as 2,4-diacetamido-2,4,6 trideoxyhexose (DATDH) or

glyceramido acetamido trideoxyhexose (GATDH) or disaccharides such as Gal α (1-3) 2,4-diacetamido-2,4,6 trideoxyhexose or Gal α (1-3) glyceramido acetamido trideoxyhexose.

Preferably, the disaccharide is not Gal α (1-3) GlcNAc.

The invention also provides fragments of the isolated mutant proteins.

Fragments may comprise 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350 or more contiguous amino acids of a mutant protein, such as a nitrite reductase or pilin protein, but less than the full-length amino acid sequence of the mutant protein.

Preferably, fragments do not comprise one or more glycosylation site residues and/or residues for ChoP addition, as hereinbefore described.

Alternatively, fragments may comprise modified glycosylation as hereinbefore described.

For example, such fragments may be produced by enzymatic cleavage of mutant proteins having modified glycosylation.

In other embodiments, chemical synthesis is optimally utilized for peptides and other protein fragments that do not exceed 60-80 contiguous amino acids in length. Peptides and protein fragments may further comprise modified glycosylation produced by chemical synthesis. Such methods are well known in the art and may be available "ready to order" from commercial sources.

In a preferred form, the aforementioned fragments are immunogenic.

More preferably, the fragments elicit an antibody response.

Even more preferably, the fragments elicit a protective immune response.

The invention also contemplates "derivatives" of the isolated mutant proteins and fragments thereof. Such derivatives may include chemical derivatives, biotinylated mutant proteins, additional amino acid sequences (such as epitope tags and fusion partners) as are well understood in the art. More detailed examples of chemical modification of proteins are provided in Chapter 15 of Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE (John Wiley & Sons Inc. NY, 1991-2008).

Fusion partners (e.g. MBP, His, GST & GFP) and epitope tags (e.g. FLAG, myc & HA) may be particularly useful for recombinant protein purification and/or detection, as is well known in the art.

The invention also provides an isolated nucleic acid encoding the isolated mutant protein of the invention, including fragments thereof.

The term "nucleic acid" as used herein designates single- or double-stranded mRNA, RNA, cRNA and DNA inclusive of cDNA and genomic DNA and DNA-RNA hybrids.

In particular embodiments, isolated nucleic acids may facilitate recombinant mutant protein production.

Accordingly, the invention provides an expression construct comprising an isolated nucleic acid the isolated mutant protein of the invention, including fragments thereof, operably linked to one or more regulatory sequences that facilitate bacterial expression of recombinant proteins and peptides.

Non-limiting examples of regulatory sequences include a bacterial origin of replication, selection marker sequences, sequences that facilitate homologous recombination, transcription and/or translation regulatory sequences and other regulatory sequences as are well known in the art.

In one particular embodiment, recombinant expression of mutant proteins may be performed using bacteria genetically

modified to lack or otherwise have altered expression of one or more enzymes involved in glycosylation and/or ChoP addition.

Examples of genes involved in glycosylation include *pgIA*, *pgIE*, *pgIG*, *pgIH*, *pgII* and *pgIL*.

An example of a gene involved in ChoP addition is *pptA*.

A more extensive description of genes involved in the glycosylation of pilin and *AniA* that may facilitate manipulation of bacterial strains to produce mutant proteins with modified or absent glycosylation are provided in Jennings et al., 1998 *Molecular Microbiology* 29:975-984; Power et al., 2000 *Microbiology* 146:967-979; Power et al., 2000 *Microbiology* 146:967-979; Power and Jennings, 2003 *FEMS Microbiology Letters* 218: 211-222; Warren et al., 2004 *FEMS Medical Microbiology and Immunology* 41:43-50; Power et al., 2006 *Biochemical and Biophysical Research Communications* 347:904-908).

Examples of bacteria for recombinant protein expression are bacteria such as *N. meningitidis*, *N. gonorrhoeae* and *E. coli* (for example DH5 α , XL1Blue, BL21(DE3), Origami and Rosetta), although without limitation thereto.

The mutant protein may be produced using genetically-modified *N. meningitidis* bacteria, particularly where modified glycosylation (as hereinbefore described) is required.

Alternatively, the mutant protein may be produced in a "standard" expression host such as *E. coli*, although without limitation thereto. This embodiment is particularly useful for the expression of isolated mutant proteins, or fragments thereof (such as set forth in SEQ ID NOS:1-9), that lack glycosylation sites.

It will also be appreciated that bacterial cells may be produced that express isolated mutant proteins of the invention, including fragments thereof, by random mutagenesis.

Chemical mutagenesis, for example, may be used to randomly mutate genes required for protein glycosylation. Mutagenized bacteria may then be selected according to an absence of glycosylation, or modified glycosylation of a glycoprotein of interest.

Bacterial cells may also be suitable for delivery of isolated mutant proteins in the context of immunogenic compositions and/or methods of eliciting an immune response. Preferably, the bacterial host is attenuated or inactivated, such as by physical, chemical or genetic means, as is well understood in the art.

One particular aspect of the invention provides antibodies which bind, recognize and/or have been raised against isolated mutant proteins of the invention, or fragments thereof.

In particular embodiments, antibodies may bind specific epitopes in a mutant pilin or mutant nitrite reductase protein of the invention.

Suitably, said antibody does not bind a corresponding wild-type glycoprotein, or glycosyl moieties thereof, or binds said wild-type glycoprotein with a lower affinity than said isolated mutant protein.

For example, the "unmasking" of isolated mutant proteins or fragments thereof may expose or otherwise reveal immunogenic epitopes that elicit a "non-native" antibody response that does not normally occur in response to the wild-type glycoprotein.

Preferably, the antibody is bactericidal and/or opsonophagocytic.

In particular embodiments, antibodies of the invention may be useful for "passive immunization" of a host against a bacterial pathogen.

Antibodies may also include antibody fragments such as Fc fragments, Fab and Fab'2 fragments, diabodies and ScFv fragments. Antibodies may be monoclonal or polyclonal.

Antibodies may be made in suitable production animal such as a mouse, rat, rabbit, sheep, chicken or goat.

Well-known protocols applicable to antibody production, purification and use may be found, for example, in Chapter 2 of Coligan et al., CURRENT PROTOCOLS IN IMMUNOLOGY (John Wiley & Sons Inc. NY, 1991-2008) and Harlow, E. & Lane, D. *Antibodies: A Laboratory Manual* (Cold Spring Harbor Laboratory, 1988).

Methods of producing polyclonal antibodies are well known to those skilled in the art. Exemplary protocols which may be used are described for example in Coligan et al., CURRENT PROTOCOLS IN IMMUNOLOGY, supra, and in Harlow & Lane, 1988, supra.

Monoclonal antibodies may be produced using standard methods, as for example described in an article by Köhler & Milstein 1975 Nature 256: 495, or by more recent modifications thereof as for example, described in Coligan et al., CURRENT PROTOCOLS IN IMMUNOLOGY, supra.

The invention also includes within its scope antibodies which comprise Fc or Fab fragments of the polyclonal or monoclonal antibodies referred to above. Alternatively, the antibodies may comprise single chain Fv antibodies (scFvs). Such scFvs may be prepared, for example, in accordance with the methods described respectively in U.S. Pat. No. 5,091,513, European Patent No 239,400 or the article by Winter & Milstein 1991 Nature 349: 293.

The antibodies of the invention may include a label selected from a group including a chromogen, a catalyst, an enzyme, a fluorophore, a chemiluminescent molecule, a lanthanide ion such as Europium (Eu³⁺), a radioisotope and a direct visual label. In the case of a direct visual label, use may be made of a colloidal metallic or non-metallic particle, a dye particle, an enzyme or a substrate, an organic polymer, a latex particle, a liposome, or other vesicle containing a signal producing substance and the like.

Several enzymes suitable for use as labels are disclosed in U.S. Pat. No. 4,366,241, U.S. Pat. No. 4,843,000, and U.S. Pat. No. 4,849,338. Suitable enzyme labels useful in the present invention include alkaline phosphatase, horseradish peroxidase, luciferase, β -galactosidase, glucose oxidase, lysozyme, malate dehydrogenase and the like. The enzyme label may be used alone or in combination with a second enzyme in solution.

Fluorophores may be selected from a group including fluorescein isothiocyanate (FITC), tetramethylrhodamine isothiocyanate (TRITC), allophycocyanin (APC), Texas Red (TR), PerCP, Cy3, Cy5 or R-Phycocerythrin (RPE). Examples of useful fluorophores may be found, for example, in U.S. Pat. No. 4,520,110 and U.S. Pat. No. 4,542,104.

In other aspects, the invention provides for the use of an agent such as an isolated mutant protein, or fragment thereof, antibodies thereto or bacterial hosts that express said isolated mutant protein, or fragment thereof, for eliciting an immune response in a host, such as a human host.

The present invention also provides immunogenic compositions which may be used therapeutically or prophylactically. Such immunogenic compositions may comprise agents such as isolated mutant proteins, fragments thereof, antibodies thereto, or bacterial hosts that express said isolated mutant protein, or fragment thereof.

Suitably, the method, use of composition, elicits a "non-native" immune response when administered to a host.

Preferably, the "non-native" immune response is a protective immune response. In such embodiments, the immunogenic composition may be a vaccine.

Immunogenic compositions may be in any of a variety of forms:

- (i) bacterial host cells engineered to express a mutant protein or fragment thereof (for example an attenuated bacterium such as *N. meningitidis*);
- (ii) a mutant protein or fragment thereof in recombinant form;
- (iii) a chemically synthesized mutant protein or fragment thereof;
- (iv) an antibody that binds or is raised against a mutant protein or fragment thereof; or
- (v) any combination of (i)-(iv).

Suitably, the immunogenic composition is administrable to an animal host, inclusive of mammals such as domestic animals, livestock, performance animals and humans.

Preferably the host is a human.

Suitably, the immunogenic composition, use and/or method elicits an immune response to one or more pathogenic bacteria. Such bacteria include *Neisseria* sp, *Campylobacter* sp, *Helicobacter* sp, *Pseudomonas* sp and *Mycobacterium* sp, although without limitation thereto.

In one particular non-limiting embodiment, it is proposed that a mutant nitrite reductase (AniA) may be particularly useful for prevention of disease caused by *N. gonorrhoeae*.

Accordingly, the immunogenic composition, use or method may prophylactically or therapeutically treat a disease or condition caused by, or otherwise associated with, an infection by said pathogenic bacterium.

Any suitable procedure is contemplated for producing immunogenic compositions, inclusive of vaccines. Exemplary procedures include, for example, those described in New Generation Vaccines (Levine et al., 1997).

The immunogenic composition of the invention may include an "immunologically-acceptable carrier, diluent or excipient".

Useful carriers are well known in the art and include for example: thyroglobulin; albumins such as human serum albumin; toxins, toxoids or any mutant cross-reactive material (CRM) of the toxin from tetanus, diphtheria, pertussis, *Pseudomonas*, *E. coli*, *Staphylococcus*, and *Streptococcus*; polyamino acids such as poly (lysine:glutamic acid); influenza; Rotavirus VP6, Parvovirus VP1 and VP2; hepatitis B virus core protein; hepatitis B virus recombinant vaccine and the like. Alternatively, a fragment or epitope of a carrier protein or other immunogenic protein may be used. For example, a T cell epitope of a bacterial toxin, toxoid or CRM may be used. In this regard, reference may be made to U.S. Pat. No. 5,785,973.

The "immunologically-acceptable carrier, diluent or excipient" includes within its scope water, bicarbonate buffer, phosphate buffered saline or saline and/or an adjuvant as is well known in the art. Suitable adjuvants include, but are not limited to: surface active substances such as hexadecylamine, octadecylamine, octadecyl amino acid esters, lysolecithin, dimethyldioctadecylammonium bromide, N,N-dicoctadecyl-N',N'bis(2-hydroxyethyl-propanediamine), methoxyhexadecylglycerol, and pluronic polyols; polyamines such as pyran, dextran sulfate, poly IC carbopol; peptides such as muramyl dipeptide and derivatives, dimethylglycine, tuftsin; oil emulsions; and mineral gels such as aluminum phosphate, aluminum hydroxide or alum; lymphokines, QuilA and immune stimulating complexes (ISCOMS).

Any safe route of administration may be employed for providing a patient with the immunotherapeutic composition of the invention. For example, oral, rectal, parenteral, sublingual, buccal, intravenous, intra-articular, intra-muscular, intra-dermal, subcutaneous, inhalational, intraocular, intrap-

eritoneal, intracerebroventricular, transdermal and the like may be employed. Intra-muscular and subcutaneous injection is appropriate, for example, for administration of immunogenic compositions and vaccines.

The above compositions may be administered in a manner compatible with the dosage formulation, and in such amount as is immunologically-effective. The dose administered to a patient, in the context of the present invention, should be sufficient to induce a beneficial response in a patient over an appropriate period of time. The quantity of agent(s) to be administered may depend on the subject to be treated inclusive of the age, sex, weight and general health condition thereof, factors that will depend on the judgement of the practitioner.

Dosage forms may include tablets, dispersions, suspensions, injections, solutions, syrups, troches, capsules, suppositories, aerosols, transdermal patches and the like. These dosage forms may also include injecting or implanting controlled releasing devices designed specifically for this purpose or other forms of implants modified to act additionally in this fashion. Controlled release may be achieved by coating the same, for example, with hydrophobic polymers including acrylic resins, waxes, higher aliphatic alcohols, polylactic and polyglycolic acids and certain cellulose derivatives such as hydroxypropylmethyl cellulose. In addition, the controlled release may be achieved by using other polymer matrices, liposomes and/or microspheres.

Compositions of the present invention suitable for oral or parenteral administration may be presented as discrete units such as capsules, sachets or tablets each containing a predetermined amount of one or more immunogenic agents of the invention, as a powder or granules or as a solution or a suspension in an aqueous liquid, a non-aqueous liquid, an oil-in-water emulsion or a water-in-oil liquid emulsion.

In a further embodiment, the isolated mutant protein may comprise modified glycosylation that includes heterologous glycosyl moieties that are normally present on other glycoproteins but not on the corresponding wild-type glycoprotein.

As demonstrated herein, the ability of glycoproteins such as wild-type pilin and nitrate reductase to elicit strong antibody responses to glycosyl moieties/glycan structures “displayed” by these glycoproteins, makes them ideal “platforms” for eliciting antibody responses to heterologous glycosyl moieties. In many cases, it is difficult to elicit antibody responses to glycosyl moieties, in which case the invention contemplates “artificially glycosylated” proteins (such as pilin or nitrate reductase, or peptides corresponding to the glycosylated regions) that facilitate generation of antibody production to the “artificial” glycosylation.

Such antibodies may have diagnostic or therapeutic use, for example in vaccines. In particular embodiments, glycosylation could be added to the protein by engineering the system into *E. coli*, or by adding glycosylation to a peptide that corresponds to the repeating pentapeptide in the C-terminus of a nitrite reductase such as AniA.

In order that the invention may be readily understood and put into practical effect, particular preferred embodiments will now be described by way of the following non-limiting examples.

EXAMPLES

Introduction

Pilin of pathogenic *Neisseria* appeared to have all of the characteristics of ideal vaccine candidates. They are required for colonization, are surface exposed and immunogenic.

However, subsequent investigations describing the specific mechanisms for high frequency changes in the amino acid sequence of the pilin glycoprotein implied that they were unsuitable as vaccine antigens. Although there is a very high frequency of sequence change in the pilin subunit protein, PilE, some short regions of conservation exist. The region of the pilin subunit that is glycosylated (Serine 63) and the glycosylated region of AniA (carboxy terminal serine containing peptide repeats) are relatively conserved with respect to amino acid substitutions associated with antigenic variation. Conservation of the underlying amino acid sequences is presumably due to maintenance of the glycosylation site. Transferases operate with a high degree of specificity and the inventors hypothesize that the conserved recognition sequences on pilin and AniA will be required for transfer to occur for both pilin and AniA glycosylation and/or ChoP modification, and/or other post-translational modifications.

In the case of AniA the extent of sequence variation amongst the sequences that are known is far less than for pilin, which is a clear example of high frequency immune evasion mechanism. In the case of AniA the data herein show an almost exclusive immune response directed towards the glycan (monosaccharide in this case from the rabbit immune data) suggests that removal of this sugar will allow a response to part of the protein other than the glycan. Our structural analysis of AniA notes that the carboxy-terminal extension on AniA from *Neisseria* is not present in other bacterial that express AniA, and is not part of the well defined active site mechanism—in fact this flexible (predicted to be flexible) C-terminal extension may “overly” these active site residues. Therefore the deletion of this region (as described in the truncation experiments in mice, may serve a two-fold purpose: 1. To remove the glycosylation by removing the target that is glycosylated (in this way there is no requirement for any PT modifications and the protein can be made in *e-coli* as described in later examples), and; 2. The removal of this flexible, repeating pentapeptide, and even larger truncations of the C-terminus (described in the *E. coli* expressed examples) may also further focus the immune response on the remained of the AniA protein that contains the key active site residues that would allow a functional blocking immune response in addition to antibodies that have other functions such as bactericidal or opsonophagocytic activities.

In *N. gonorrhoeae* this protein is expressed by all strains tested, and does not have the silencing mutations we have found in *N. meningitidis* (where ~30% of clinical isolates do not express the protein at all). Further, in *N. gonorrhoeae*, the function of AniA is a key for formation of biofilms, so generation of these functional blocking antibodies is anticipated to have a similar response to the mutation. Finally, in the latter examples we have proposed removal of N-terminal regions of AniA in addition to the C-terminal regions. We note that the N-terminal region of AniA from *Neisseria* is not present in other bacterial that express AniA, and, like the C-terminal extension is not part of the well defined active site mechanism—in fact this flexible (predicted to be flexible) N-terminal extension is the site where a lipid modification is added (*Neisseria* AniA is a lipoprotein) to anchor the bacterial to the membrane (in other bacteria AniA is not a lipoprotein), therefore the deletion of this N-terminal region, in addition to the C-terminal region may further direct the immune response to the conserved, regions required for AniA function.

Thus, a conserved amino acid sequence, usually masked by a glycan and/or ChoP, if presented without the overlying structure, may elicit antibodies of novel specificity that can recognize the conserved epitopes on pilin and AniA regardless of the post-translational modification.

Example 1

Vaccines Comprising Glycosylation Modified Mutant Pili

The glycosylated region of pilin is proposed to be on the surface of the pilus structure and has a relatively conserved amino acid sequence, hence the present inventors hypothesis that the removal of immunogenic and variable structures from pilin such as sugars and ChoP may elicit "non-native" immune responses against subsequent infection. Specifically, the substitution of trisaccharides for shorter mono- or disaccharides on pilin protein or pilin devoid of glycosylation is hypothesized to promote a novel antibody response not generated with wild-type pili.

Reference is made to Power et al., 2003 *Mol Microbiology*, 49: 833; Power et al., 1999 *Microbiology* 145: 3013; Jennings et al., 1998 *Mol Microbiology* 29: 975; Power and Jennings, 2003 *FEMS Microbiology Letters* 218: 211-222; Warren et al., 2004 *FEMS Medical Microbiology and Immunology* 41:43-50; Power et al., 2006 *Biochemical and Biophysical Research Communications* 347:904-908, which describe characterization of the *pglA*, *pglB*, *pglC*, *pglD*, *pglE*, *pglF* and *pglI* genes, that play specific and important roles in the biosynthesis of pilin glycans having a terminal galactose as part of a Gal β (1-4)Gal(α 1-3)DATDH structure and, in some cases, in biosynthesis of the disaccharide Gal(α 1-3)GlcNAc. Furthermore, the basal sugar that is O-linked to Serine, DATDH, can be modified depending on whether the strain expressing the pilin has the *pglB1* or *pglB2* allele (Power et al., 2003 *Molecular Microbiology* 49: 833; Chamot-Rooke et al., 2007 *PNAS* 104: 14783-14788), and whether *pglI* is phase varied ON or OFF (Warren et al., 2004, *FEMS Medical Microbiology and Immunology* 41:43-50; Chamot-Rooke et al., 2007, *PNAS* 104: 14783-14788).

The present invention provides a pilin peptide epitope comprising a relatively conserved peptide and a truncated oligosaccharide structure. Preferably, the truncated oligosaccharide is a monosaccharide (either a 2,4-diacetimidido-2,4,6-trideoxyhexose or variant structure based on *PglB* allele and *PglI* expression) linked at serine 63 to a short peptide comprising the conserved amino acid sequence that underlies the glycosylation site. Those epitopes which are found present in all strains expressing pili and elicit functional antibodies, will be incorporated into vaccines.

Suitable glycopeptides are produced using the His-tagged pilin (Dieckelmann, et al., 2003 *Protein Expression and Purification* 30:69-77) or FLAG-tagged expression system in strain C311*pglA* and a strain expressing and alternate basal sugar structure such as strain 8013 SB *pglA*. These strains will express the minimal monosaccharide structures. In some embodiments, proteins may be cleaved with trypsin to release a 28 amino acid peptide. The peptides may be purified by HPLC, the identity and purity confirmed by ESI-MS and used in two separate approaches:

Example 2

PilE::Flag Construction

Flag-tag was chosen as an alternative tag system to purify pilin. Flag-tag, also called Flag octapeptide, consists of eight amino acids (DYKDDDDK) that bind to the commercially available monoclonal antibodies M1 and M2 with high specificity. The tag was fused at the C-terminus of PilE to avoid interference with secretion. To fuse the Asp-Tyr-Lys-Asp-Asp-Asp-Lys (M2 Flag) tag to the C-terminus of the

chromosomally located pilE gene of C311#3, the construct pGEMTetMBpilE::Flag/lpxC was constructed to facilitate the tagging of the PilE protein. The pilE gene was amplified from strain C311#3 using the primers PilE-NotI (5'-GACCTG-CAGGCGGCCGCGAATTCCTACTA-3') and Flag-XhoI (5'-TTAAACTC-GAGCTTATCGTCGTCATCCTTGTAATCGCTAGCATCACTTGGCTCGGGCAGG-3'). The Flag-XhoI primer has Flag tag and XhoI digestion site extension to allow incorporation of the tag in-frame with pilE. The resulting pilE::Flag DNA fragment was and ligated to pGEMTetMpileMCS/lpxC to have pGEMTetMBpilE::Flag containing the correct orientation of pilE::Flag.

This plasmid pGEMTetMBpilE::Flag/lpxC, contains the pilE gene with a Flag-tag, a tetracycline cassette used as a selectable marker, an intergenic region, and part of a gene downstream of pilE on the chromosome to allow homologous recombination to occur as shown. The construct was linearised with NotI and transformed into C311#3. Transformants in which the pilE::Flag allele had replaced the pilE region on the chromosome were selected by growth on BHI containing 5 μ g/ml tetracycline. This resulted in the tagged allele being transferred to the chromosome of *N. meningitidis* C311#3. The plasmid pGEMTetMBpilE::Flag/lpxC was also transformed into glycosylation and phosphorylcholine mutants C311*pglA* (Jennings et al., 1998 *Molecular Microbiology* 29:975-984), C311*pptA* (Warren and Jennings, 2003 *Infection and Immunity* 71:6892-68928) and C31126*ApplA* (Warren and Jennings, 2003) to have C311pilE::Flag C311*pglA*/pilE::Flag, C311*pptA*/pilE::Flag and C31126*ApplA*/pilE::Flag.

Flag-Tagged Pilin Purification

Heavily inoculated confluent cultures of C311#3pilE::Flag were grown overnight on large BHI plates (135-mm diameter; 5 plates). Each large plate of cells was harvested into 15 ml TE buffer (10 mM Tris-Cl, pH 7.5, 1 mM EDTA) and heat-killed for 1 h at 56° C. Complete EDTA-free Protease Inhibitor Cocktail was resuspended according to manufacturer's instructions (Roche), and the cells were French-pressed five times at 1000 psi gauge pressure. The lysate was centrifuged twice at 14,000 g for 30 min at 4° C. The supernatant was collected, filtered through a 0.22- μ m filter (Amicon), and applied to an anti-flag affinity gel column for Flag-tagged protein purification. The entire 15 ml supernatant was loaded on a 15 ml column volume with 1 ml of anti-flag ANTI-FLAG® M2 Affinity Gel (Sigma) that had been washed with TBS buffer (50 mM Tris HCl, 150 mM NaCl, pH7.4). The binding of Flag-tagged pilin to resin was incubated on the rotor in 4° C. for overnight. The column was subsequently washed with twenty column volumes of TBS buffer and Flag-tagged pilin was eluted with eight 1 ml aliquots of 0.1M Glycine HCl (pH3.5) into vials containing 20 μ l of 1M Tris, pH8.0. Purified Flag-tagged pilin (antigen for mouse immunization) from C311pilE::Flag C311*pglA*/pilE::Flag, C311*pptA*/pilE::Flag and C31126*ApplA*/pilE::Flag was analyzed as shown in FIG. 1. Purified antigen were used to immunize Balb/C mice (mice, 10 per group, vaccinated with 5 μ g of protein/peptide+Adjuvant (Freunds) at days 0, 21 and 28 and sacrificed on day 35.

Antigen Preparation for Western Blot Analysis

Pilin was prepared based on previously described methods (Virji, 1993 *Molecular Microbiology* 10:1013-1028). The cells from a plate of overnight growth were added to 500 μ l of PBS. The pili were sheared off the outside of the cells by vortexing vigorously for 1 min and the cells were removed from the mixture by centrifuging at 12,000 g in a bench-top centrifuge for 15 min. The supernatant was transferred to a new tube and incubated at 56° C. for 1 hr to kill any remaining cells.

Vortex pilin from C311 WT, C311pglA (Jennings et al., 1998), C311pptA (Warren and Jennings, 2003) and C31126ApglA (Warren and Jennings, 2003) were balanced by western probed by anti-pilin as shown in FIG. 2. The balanced samples were analyzed by western with the antiserum. In FIG. 2, the number 16-35 represents the mouse number. Mice 16-20 were immunized with C311 WT Flag-tagged pilin. Mice 21-25 were immunized with C311pglA Flag-tagged pilin. Mice 26-30 were immunized with C311pptA Flag-tagged pilin. Mice 31-35 were immunized with C31126ApglA Flag-tagged pilin.

Example 3

Development of Monoclonal Antibodies to Define Protective, Conserved Epitopes

Experiments to develop monoclonal antibodies using Balb/C mice for the production of monoclonal antibodies (mAbs; 5 per group, vaccinated with 5 µg of pure protein or peptide+MPL, boosted to high titre) are scheduled. The antigens used in ELISA to identify anti-pili mAbs will be whole cells of C311#3 and C311#3pilE::kan, which do not express pilin. In order to find a sub-set of mAbs that have an epitope consisting of or including the ChoP modification site, purified pilin from C311#3 and derivatives of this strain that have a site directed mutation which removes the ChoP modification site (as above) will be used. Routine procedures of splice overlap PCR to make site-directed changes to pilin sequence are then performed. MABs of the appropriate specificity may be tested in a number of ways:

1. Whole cell ELISA on large collections of strains to determine the proportion of strains that express a particular epitope. A C311#3pilE::kan mutant strain serves as the negative control. If no binding is observed in a particular strain, confirmation may be made that the strain is expressing pilin by EM.
2. Bactericidal killing (BC) assays on capsulate *N. meningitidis* C311#3 and a range of heterologous strains to determine the BC titre for each monoclonal (eg. Hoogerhout et al., 1995) may be conducted.
3. Opsonophagocytic assays on capsulate *N. meningitidis* C311#3 plus a range of heterologous strains using methods described in Pledsted et al., 1999 may be conducted.
4. If this approach yields mAbs that define candidate epitopes and have BC or opsonophagocytic activity, then development of the antigen to optimize the production of the desired specificity follows. Characteristics such as size of peptide, conjugations to a carrier and adjuvant systems are then ascertained.

In preliminary experiments, monoclonal antibodies specific for pilin glycosylation structures have been raised. Balb/C mice were immunised with wild type pilin expressed as a HIS tagged molecule in *Neisseria* that retains post-translational modifications (Dieckelmann et al., 2003 Protein Expression and Purification 30:69). Hybridomas were first screened in whole cell ELISA against wild-type, strain C311#3, or C311#3pilE::kan which does not express pilin. Hybridomas specific for “pili antigens” were then subject to secondary screening, again using whole cell ELISA, but this time with wild-type C311#3 and a panel of C311#3 mutants strains expressing pilin with various defects in glycosylation. Reactivity with wild type C311#3 that is lost in a specific mutant indicates that the glycan structure absent in that mutant is required for monoclonal antibody recognition and may indicate a monoclonal antibody specific for a particular

glycan structure. Of the 183 hybridomas recognizing “pili antigens” that were screened, none were directed at oligosaccharide structures.

However, in secondary studies, the same set of 183 hybridomas against wild type C311#3 which expresses ChoP on pilin and the C311#3 phase variant, 26A, which lacks ChoP were screened. The inventors reasoned that this process may result in an anti-ChoP monoclonal antibody that may have characteristics superior to TEPC-15. Unexpectedly, 180/183 antibodies lost reactivity with pilin expressed by the 26A variant, the 26A phase variant being derived from C311#3. This variant expresses pilin on the surface of the cell at the same level as wild type (as determined by whole cell ELISA and EM). It has an identical pilin subunit amino acid sequence as the wild type strain and retains wild type glycosylation. The only difference between wild type and 26A detectable was the absence of the ChoP structure. The inventors interpretation of this data, derived from hybridomas from fusions from several different mice, is that either the ChoP epitope(s) elicits a disproportionately strong immune response compared to polypeptide and oligosaccharide epitopes in the same molecule or the position of the ChoP on pilin (unknown) is surface exposed and is preferentially recognized in whole cell ELISA or a combination of these two factors. In either case, these significant results indicate that ChoP is an important factor in immune response to and immune recognition of pilin on the surface of *Neisseria*. As expression of the ChoP on pilin can randomly switch on and off, the immune response elicited against epitopes comprised of ChoP may represent a mechanism of immune evasion.

Immunogenicity Trial

The same antigens used above in the development of monoclonal antibodies are scheduled for antigenicity trials to determine whether a short cut (cf. the development of monoclonal antibodies) can be taken by determining if antibodies of desired specificity are generated in polyclonal sera. Antigen (both pure protein and unmodified peptide, described above) from C311#3 and C311#3 pptA will be used to immunize Balb/C mice (mice, 10 per group, vaccinated with 5 µg of protein/peptide+MPL (or similar adjuvant—we used Freund's in the rabbit and mouse experiments) at days 0, 21 and 28 and sacrificed on day 35). Immune response is monitored by ELISA, as above, and by Western blot analysis. The serum produced is tested in BC assay with the capsulate, wild-type C311#3 and the derivative that expresses pilin that lacks the ChoP modification site region. Differences in titre between these two will be due to the action of ChoP modification site-specific antibodies in the polyclonal sera. If data suggest that beneficial antibodies are being produced, then improvements to the response using the approaches described above will be sought. Heterologous strains that express the same basal (serine-linked) monosaccharide in their wild-type structure, but with significant amino acid sequence differences (outside the core, conserved region underlying the glycosylation site) will be selected. In this way, the assay will be biased towards detection of antibodies with BC activity that recognize epitopes comprised of both peptide and saccharide. If data suggest that beneficial antibodies are being produced, then improvements to the response using in the approaches described above will be sought.

Example 4

We have identified AniA, an anaerobically induced nitrite reductase, which is glycosylated by the same pathway. This demonstrates that the pilin glycosylation pathway is a general pathway for O-glycosylation in pathogenic *Neisseria*. AniA

is known to be an immunogenic outer membrane protein, and glycosylation of this protein with the same phase variable structure that is found on pilin may serve an immunoevasion role. Removal or modification of the glycan or the glycosylated region may lead to a non-native, protective immune response.

Identification of AniA as a Glycoprotein

Western blotting using anti-trisaccharide antisera (Power et al., 2003 Molecular Microbiology 49: 833) revealed a high molecular weight band in strain C311 that disappeared in a C311pglA strain (FIG. 3A; glycosylation pathway mutant), suggesting that there was an additional glycoprotein to pilin which migrates at ~17 kDa. This band was still present in a C311pilE mutant strain (cannot make pilin) therefore the glycoprotein could not be aberrantly migrating pilin (FIG. 3A). To identify the protein the region of the gel containing the reactive protein was isolated and subject to tryptic cleavage and peptide mass analysis by mass spectrometry. Three candidate proteins were identified: PorA, the major outer membrane porin of *N. meningitidis*, FrpB, an outer membrane protein required for iron uptake, and AniA an outer membrane protein with nitrite reductase activity.

Mutations were made in each candidate gene and these mutant alleles transferred to the chromosome using established methods (eg. Power et al., 2003 Molecular Microbiology 49: 833). The band identified by the anti-trisaccharide sera was still present in the C311porA and C311frpB mutant strains (FIGS. 3B and 3C, respectively) but was lost in the C311aniA mutant, indicating that AniA may be the glycoprotein (FIG. 3D). Using an anti-AniA antibody (Cardinale et al., 2000 Infection and Immunity 68: 4368) it was demonstrated that the C311aniA mutant did not express AniA (FIG. 3E). In a series of mutants in the pilin glycosylation pathway, pglE, pglA and pglB, which result in truncation of the pilin linked glycan from a trisaccharide (wild type C311) to a di-saccharide (C311pglE) to a monosaccharide (C311pglA) to no saccharide (C311pglB), the AniA protein has a stepwise reduction in apparent molecular weight (FIG. 3F) consistent with it being a glycoprotein that is post-translationally modified by the same pathway as pilin. A similar increased migration is seen when AniA of *N. gonorrhoeae* is examined by Western blot in wild type strain 1291, compared to 1291pglA (monosaccharide) and 1291pglD (no glycosylation) (FIG. 3G). This indicates that AniA is also a glycoprotein in *N. gonorrhoeae*.

Sequencing of 41 *N. meningitidis* strains revealed that 38% of strains contained a frame shift mutation that would result in premature termination of the protein. Typical examples are shown in FIG. 4A. Analysis of two of the *N. meningitidis* strains containing the frame shift mutation, 1000 and NGP20, revealed that these strains did not express the AniA protein in Western blot analysis (FIG. 4B) and did not have nitrite utilization activity and behaved like a C311aniA mutant (FIG. 4C). This suggests that all other strains with the same allele also lack AniA expression, indicating that AniA expression has been lost in a significant minority of *N. meningitidis* isolates. In contrast, all *N. gonorrhoeae* strains tested had the wild type allele, suggesting that AniA has a key role in *N. gonorrhoeae* biology.

Comparison of the deduced amino acid sequence of the 41 *N. meningitidis* strains reveals a number of differences. These are shown graphically in FIG. 4E (data compiled from FIGS. 5A and 5B). Examination of the position of these differences (Red; FIG. 4FGH), show that they are all on the outer face of the protein, suggesting they may have been generated for by

immune selective pressure. Furthermore, theoretical translations of the strains containing the frame shifted AniA gene reveal further differences also on the outer face of the protein (Orange; FIG. 4FGH).

Taken together, these data suggest that immune selective pressure has selected for both the amino acid sequence polymorphisms and silencing of the gene in 38% of *N. meningitidis* strains. The conservation that this protein is glycosylated by a phase variable glycan via the same pathway as pilin adds further evidence that this protein may be under immune selection. The glycosylation is not required for AniA function, as a truncated glycan expressed by AniA in a C311pglA strain has no difference in nitrite utilization activity compared to wild type C311 (see FIG. 4C).

AniA is Glycosylated in the Carboxy Terminal Region.

In order to investigate the location of the glycosylation of AniA, an AniA::flag tag fusion was made and placed on the chromosome to allow expression and affinity purification of AniA from various mutant backgrounds. The approach used was the same as in previous studies with 6xHIS-tagged pilin (Dieckelmann et al., 2003 Protein Expression and Purification 30:69-77) except the flag peptide (DYKDDDDK) was used instead of 6xHIS. MS analysis confirmed that there were multiple glycans covalently linked to a C-terminal peptide consisting of a repeating tetrapeptide (see FIG. 6B). One of the residues in the repeating peptides is serine, and these serines are the only possible candidates for the location of the O-linked glycan.

The crystal structure of AniA was determined using a recombinant protein expressed in *E. coli* that had the N- and C-regions deleted, including the glycosylated region, so there is no structural data on this domain of the AniA protein. However, the C-terminus (cyan; FIG. 4FGH) does emerge from the "core protein" in a cleft adjacent to the majority of the observed amino acid sequence polymorphisms, and may indicate that the C-terminus is exposed on the surface of the wild type AniA protein. Whole cell ELISA (FIG. 7A) and colony immunoblot (FIG. 7B) of cells indicated that the AniA protein is exposed on the surface of the bacterial cell.

Vaccines Comprising Glycosylation Modified Mutant AniA.

AniA of pathogenic *Neisseria* is known to be immunogenic protein, and may have key roles in anaerobic growth. An immune response against AniA may be effective in preventing disease or colonization of the host by inducing antibodies with bactericidal or opsonophagocytic activity. An immune response directed at AniA may also induce antibodies with functional blocking activities. The discovery that AniA is a glycoprotein, and that it is likely that the covalent linkage of a surface exposed phase variable glycan may act as a mechanism for immunoevasion, provides opportunities to develop recombinant antigens that will elicit a non native immune response. These antigens may be of several types. Firstly, the full length AniA protein expressed in *Neisseria* that is affinity purified (as above), or AniA enriched membrane vesicle where AniA is expressed from a strong promoter, or fragments of AniA expressed in *Neisseria* or generated by proteolytic cleavage after purification. AniA may also be expressed in a heterologous expression system like *E. coli*. In this system, if post-translational modifications are required pgl genes may be expressed in *E. coli* to provide desired components of the glycosylation pathway. The AniA antigen may also be made as a synthetic peptide.

To generate a non-native response to conserved epitopes, AniA antigens with truncated glycans may be prepared. One example is a monosaccharide where AniA antigen can be purified from a set of strains that make all 4 known variations of the basal sugar that is O-linked to Serine. For example

DAIDH can be modified depending on whether the strain is expressing the *pglB1* or *pglB2* allele (Power et al., 2003 *Molecular Microbiology* 49: 833; Chamot-Rooke et al., 2007 *PNAS* 104: 14783-14788), and whether *pglI* is phase varied ON or OFF (Warren et al., 2004 *FEMS Medical Microbiology and Immunology* 41:43-50; Chamot-Rooke et al., 2007 *PNAS* 104: 14783-14788).

A further example is an AniA antigen expressed with no glycans, either from *pglF* or *pglL* or similar *Neisseria* strains, or from *E. coli*, which lacks the glycosylation pathway.

Another further example is an AniA antigen where all or part of the C-terminal glycosylated region is deleted to remove the variable antigen portion of the protein.

Example 5

Construction and Expression of FLAG-Tagged AniA from *N. meningitidis* Strain C311

Sequence encoding a FLAG tag (N-Asp-Tyr-Lys-Asp-Asp-Asp-Lys-C) was inserted at the C-terminus of the *aniA* gene in C311. Vector pT7blueaniA::flagtetMB was constructed by overlap PCR using the primers *aniA_F*, *NMB1624_R*, 3' *flag_XhoI_ds* and *NMB1624_F_XhoI*. The 3' *flag_XhoI_ds* primer encoded a FLAG-tag extension followed by a stop codon to allow incorporation of the tag in frame with *aniA*. The *aniA::flag* construct with *NMB1624* (downstream of *aniA*) was initially cloned into pT7blue (Novagen) to create pT7blueaniA::flag. A tetracycline antibiotic resistant cassette (TetMB) was digested with *Sall* and cloned into *XhoI* linearised pT7blueaniA::flag to create pT7blueaniA::flag tetMB, which was transformed to the chromosome of C311 by homologous recombination as described (Jennings et al., 1995 *Microb Pathol* 19: 391-407). The genomic DNA of pT7blueaniA::flag tetMB was transformed to C311#3pglA and C311#3pglL using the above method for AniA with truncated glycan (i.e. monosaccharides and no glycan respectively). Expression of FLAG-tagged truncated AniA was achieved with the same approach described above but using primer *aniA3'flag_trunc2* instead of 3'*flag_XhoI_ds*. The truncated FLAG-tagged AniA is shown in FIG. 9.

Characterisation of Antigen for Animal Immunization.

The FLAG-tagged AniA antigen and the truncated FLAG-tagged AniA antigen were purified according to manufacturer's instruction with 3% of Tween 20. The antigens purified are characterised with Western blot analysis using anti-FLAG, anti-AniA mAb and anti-trisaccharide sera (FIG. 9). Rabbit Immunogenicity Trial.

Production of antisera specific for AniA with truncated glycosylation (AniA-PglA) were raised in rabbit, as essentially described in Power et al. (2000 *Microbiology* 146: 967-979). AniA-PglA antigen is prepared as described above. The immune response was monitored by Western blot analysis (FIG. 10).

Mouse Immunogenicity Trial.

Production of antisera specific for AniA with truncated glycan (AniA-PglA), deglycosylated AniA (AniA-PglL) and truncated AniA were raised in mice. In brief, purified AniA antigen from truncated glycan strains (C311pglA and C311pglL) will be used to immunise Balb/C mice (Mice, 5 per group, vaccinated with 5 ug of protein+Freunds at days 0, 21 and 28 and sacrificed on day 35). The immune response was monitored by western blot analysis.

In Vivo Nitrite Utilisation Assays.

Cells may be grown to OD 0.5 A_{600} , washed once in PBS containing 27.8 mM glucose, then resuspended to an OD of 1

in 10 ml of the same solution. After equilibration at 37° C. for 30 mins, heat-inactivated mouse antiserum may be added in 1/100 dilution and NaNO₂ was added to the cultures to a final concentration of 1 mM. Nitrite utilization may be assayed colourimetrically with the Griess reagent (Green et al., 1982 *Biochem.* 126: 131-138) essentially as described by Anjum et al. (2002 *J Bacteriol.* 184: 2984-2993). 100 µA of each sample is collected for assay every 10 min for 1 hour. 50 µl of 1% sulphanimide was added to the samples, and the reaction is started with the addition of 100 µl of a 0.02% solution of N-naphthylenediamine. The reaction is followed by measuring absorbance at 540 nm.

Results

The data shown in FIGS. 11 and 12 demonstrate that as predicted, glycosylated AniA elicited a strong antibody response. More particularly, this antibody response was largely directed to glycosyl moieties, even in the case of AniA proteins having modified glycosylation (eg. in C311 *pglA* and *pglL* bacteria). Most striking was the strong antibody response to the truncated AniA protein lacking glycosylation (SEQ ID NO:1). Antibodies generated by this response (Antiserum B) recognized AniA independently of the presence or absence of AniA glycosylation.

Example 6

Given the results in Examples 5 which demonstrated the immunogenicity of truncated AniA protein fragments completely lacking glycosylation, it is proposed that such fragments may be readily expressed in "standard": expression bacterial host cells such as *E. coli* that do not glycosylate the protein. This obviates the need to use more specialized bacteria (such as the genetically-modified *N. meningitidis* strains mentioned previously) that can partially-glycosylate the protein.

Expression of Truncated AniA in *E. coli*

Truncated AniA proteins were amplified from *N. gonorrhoeae* strain 1291 using primers listed in tableXX. Truncated AniA #1 were amplified using primers *ExpAniA_NdeI_F* and *ExpAniA_BamHI_E_R*; Truncated AniA #2 using *ExpAniA_NdeI_F* and *ExpAniA_BamHI_M_R*; Truncated AniA #3 using *ExpAniA_NdeI_F* and *ExpAniA_BamHI_G_R*; Truncated AniA #4 using *ExpAniA_NdeI_F* and *ExpAniA_BamHI_Y_R*; Truncated AniA #5 using *ExpAniA_NdeI_E_F* and *ExpAniA_BamHI_E_R*; Truncated AniA #6 using *ExpAniA_NdeI_E_F* and *ExpAniA_BamHI_M_R*; Truncated AniA #7 using *ExpAniA_NdeI_E_F* and *ExpAniA_BamHI_G_R*; Truncated AniA #8 using *ExpAniA_NdeI_E_F* and *ExpAniA_BamHI_Y_R*. The amplified sequences encoding truncated AniA is cloned into pET15b expression vector (Novagen) with *NdeI* and *BamHI* sites. The truncated HIS-tagged AniA will be purified and his-tag will be cleaved with protease thrombin.

The encoded protein sequences are set forth in SEQ ID NOS:2-9 (FIG. 13).

These non-glycosylated, AniA protein fragments will be tested for immunogenicity as previously described in Example 5.

It will be appreciated by the skilled person that the present invention is not limited to the embodiments described in detail herein, and that a variety of other embodiments may be contemplated which are nevertheless consistent with the broad spirit and scope of the invention.

It will be further appreciated that the principle set forth herein is applicable to any post-translationally modified protein of any pathogenic bacterium.

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All patent and scientific literature and computer programs referred to in this specification are incorporated herein by reference in their entirety.

Tables

TABLE 1

Primer sequences	
Primer Name	Sequence (5'→3')
aniA_F	ATGAAACGCCAAGCCTTAG
NMB1624_R	TTATCGGCTTGTGCAACGGAAGCCC
3'flag_XhoI_ds	AATAACCGGACATACTTCATCTCGAGTCACT TGTCGTCATCGTCCTTGTAGTCATAAACGCT TTTTTCGGATGCAGAGGC
NMB1624_F_XhoI	CTCGAGATGAAGTATGTCCGGTTATTTTTCC
aniA3'flag_trunc2	TTCATCTCGAGTCACTTGTGTCATCGTCCT TGTCGTCATAAACCATGATTTTCAGGGTTTTTC TGC

24

TABLE 2

Primer sequences	
Primer Name	Sequence (5'→3')
ExpAniA_NdeI_F	CGCACTCATATGCCGCACAAGCTACCGCCGAA
ExpAniA_NdeI_E_F	CGCACTCATATGAACTGCCCGTCATCGAT
ExpAniA_BamHI_E_R	GCGTCCGGATCCCTTACTTCTACTTTCAATTGCC
ExpAniA_BamHI_M_R	GCGTCCGGATCCCTTACATGATTTTCAGGGTTTTTC
ExpAniA_BamHI_G_R	GCGTCCGGATCCCTTAGCCGCTGCCGGCGTAAGC
ExpAniA_BamHI_Y_R	GCGTCCGGATCCCTTATTAATAAACGCTTTTTTC

*Restriction site is indicated by underlying letter.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 113

<210> SEQ ID NO 1

<211> LENGTH: 362

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Truncated FLAG-tagged AniA.

<400> SEQUENCE: 1

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
1 5 10 15

Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Glu Thr Pro
20 25 30

Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu
35 40 45

Thr Pro Ser Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
50 55 60

Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
65 70 75 80

Val Lys Met Glu Thr Val Glu Lys Thr Met Thr Met Glu Asp Gly Val
85 90 95

Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
100 105 110

Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
115 120 125

Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
130 135 140

Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
145 150 155 160

Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
165 170 175

Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
180 185 190

-continued

Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 195 200 205
 Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 210 215 220
 Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 225 230 235 240
 Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 245 250 255
 Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 260 265 270
 Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 275 280 285
 Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 290 295 300
 Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
 305 310 315 320
 Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn
 325 330 335
 Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 340 345 350
 Ile Met Asp Tyr Lys Asp Asp Asp Asp Lys
 355 360

<210> SEQ ID NO 2
 <211> LENGTH: 309
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria gonorrhoea

<400> SEQUENCE: 2

Gly Ser His Met Ala Ala Gln Ala Thr Ala Glu Thr Pro Ala Gly Glu
 1 5 10 15
 Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro Pro
 20 25 30
 Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr
 35 40 45
 Val Glu Lys Thr Met Lys Met Asp Asp Gly Val Glu Tyr Arg Tyr Trp
 50 55 60
 Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly
 65 70 75 80
 Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro
 85 90 95
 His Asn Val Asp Phe His Ala Ala Thr Gly Gln Gly Gly Ala Ala
 100 105 110
 Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala
 115 120 125
 Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly
 130 135 140
 Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys
 145 150 155 160
 Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp
 165 170 175
 Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp
 180 185 190
 Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly
 195 200 205

-continued

His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly
 210 215 220
 Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser
 225 230 235 240
 Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly
 245 250 255
 Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly
 260 265 270
 Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile Pro Gly Asn Tyr Thr
 275 280 285
 Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly
 290 295 300
 Gln Leu Lys Val Glu
 305

<210> SEQ ID NO 3
 <211> LENGTH: 317
 <212> TYPE: PRT
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<400> SEQUENCE: 3

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 1 5 10 15
 Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro Pro
 20 25 30
 Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr
 35 40 45
 Val Glu Lys Thr Met Lys Met Asp Asp Gly Val Glu Tyr Arg Tyr Trp
 50 55 60
 Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly
 65 70 75 80
 Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro
 85 90 95
 His Asn Val Asp Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala
 100 105 110
 Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala
 115 120 125
 Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly
 130 135 140
 Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys
 145 150 155 160
 Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp
 165 170 175
 Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp
 180 185 190
 Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly
 195 200 205
 His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly
 210 215 220
 Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser
 225 230 235 240
 Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly
 245 250 255
 Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly

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Leu Ser Asp Thr Ala Tyr Ala Gly Ser Gly
325 330

<210> SEQ ID NO 5
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 <212> TYPE: PRT
 <213> ORGANISM: Neisseria gonorrhoea

<400> SEQUENCE: 5

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20 25 30
 Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr
35 40 45
 Val Glu Lys Thr Met Lys Met Asp Asp Gly Val Glu Tyr Arg Tyr Trp
50 55 60
 Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly
65 70 75 80
 Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro
85 90 95
 His Asn Val Asp Phe His Ala Ala Thr Gly Gln Gly Gly Glu Ala Ala
100 105 110
 Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala
115 120 125
 Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly
130 135 140
 Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys
145 150 155 160
 Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp
165 170 175
 Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp
180 185 190
 Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly
195 200 205
 His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly
210 215 220
 Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser
225 230 235 240
 Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly
245 250 255
 Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly
260 265 270
 Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile Pro Gly Asn Tyr Thr
275 280 285
 Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly
290 295 300
 Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu Ile Met Thr Gln Lys
305 310 315 320
 Leu Ser Asp Thr Ala Tyr Ala Gly Ser Gly Ala Ala Ser Ala Pro Ala
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 Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Ser Glu Lys
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 Ser Val Tyr
355

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<210> SEQ ID NO 6
 <211> LENGTH: 298
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria gonorrhoea

<400> SEQUENCE: 6

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 20 25 30
 Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp Gly Val
 35 40 45
 Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 50 55 60
 Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 65 70 75 80
 Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
 85 90 95
 Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
 100 105 110
 Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
 115 120 125
 Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
 130 135 140
 Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 145 150 155 160
 Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 165 170 175
 Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 180 185 190
 Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 195 200 205
 Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 210 215 220
 Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 225 230 235 240
 Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 245 250 255
 Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
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 Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 290 295

<210> SEQ ID NO 7
 <211> LENGTH: 306
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria gonorrhoea

<400> SEQUENCE: 7

Gly Ser His Met Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
 1 5 10 15
 Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
 20 25 30

-continued

Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp Gly Val
 35 40 45
 Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 50 55 60
 Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 65 70 75 80
 Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
 85 90 95
 Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
 100 105 110
 Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
 115 120 125
 Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
 130 135 140
 Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 145 150 155 160
 Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 165 170 175
 Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 180 185 190
 Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 195 200 205
 Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 210 215 220
 Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 225 230 235 240
 Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 245 250 255
 Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
 260 265 270
 Pro Gly Asn Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn
 275 280 285
 Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 290 295 300
 Ile Met
 305

<210> SEQ ID NO 8
 <211> LENGTH: 319
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria gonorrhoea

<400> SEQUENCE: 8

Gly Ser His Met Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
 1 5 10 15
 Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
 20 25 30
 Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp Gly Val
 35 40 45
 Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 50 55 60
 Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 65 70 75 80
 Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln

-continued

Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 145 150 155 160

Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 165 170 175

Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 180 185 190

Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 195 200 205

Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 210 215 220

Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 225 230 235 240

Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 245 250 255

Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
 260 265 270

Pro Gly Asn Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn
 275 280 285

Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 290 295 300

Ile Met Thr Gln Lys Leu Ser Asp Thr Ala Tyr Ala Gly Ser Gly Ala
 305 310 315 320

Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala
 325 330 335

Ser Ala Ser Glu Lys Ser Val Tyr
 340

<210> SEQ ID NO 10
 <211> LENGTH: 19
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 10

atgaaacgcc aagccttag

19

<210> SEQ ID NO 11
 <211> LENGTH: 25
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 11

ttatcggcctt gtgcaacgga agccc

25

<210> SEQ ID NO 12
 <211> LENGTH: 80
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 12

aataaccgga catacttcat ctcgagtcac ttgtcgtcat cgtccttgta gtcataaacg

60

cttttttcgg atgcagaggc

80

<210> SEQ ID NO 13

-continued

<211> LENGTH: 31
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 13
 ctcgagatga agtatgtccg gttatttttc c 31

<210> SEQ ID NO 14
 <211> LENGTH: 65
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 14
 ttcatctcga gtcactgtgc gtcacogtcc ttgtagtcat aaacctgat ttcagggttt 60
 tctgc 65

<210> SEQ ID NO 15
 <211> LENGTH: 32
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 15
 cgcaactcata tgccgcacaa gctaccgccc aa 32

<210> SEQ ID NO 16
 <211> LENGTH: 29
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 16
 cgcaactcata tgaactgccc gtcacogat 29

<210> SEQ ID NO 17
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 17
 gcgtccggat ccttactcta ctttcaattg ccc 33

<210> SEQ ID NO 18
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 18
 gcgtccggat ccttacatga tttcagggtt ttc 33

<210> SEQ ID NO 19
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence.

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<400> SEQUENCE: 19
gcgtccggat ccttagccgc tgccggcgta agc 33

<210> SEQ ID NO 20
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Primer sequence.

<400> SEQUENCE: 20
gcgtccggat ccttattaat aaacgctttt ttc 33

<210> SEQ ID NO 21
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 21
atggaaaccg tcgaaaaaac catgaccatg gaa 33

<210> SEQ ID NO 22
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 22
atggaaaccg tcgaaaaaac catgaccatg gaa 33

<210> SEQ ID NO 23
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 23
atggaaaccg tcgaaaaaac catgaccatg gaa 33

<210> SEQ ID NO 24
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 24
atggaaaccg tcgaaaaaac catgaccatg gaa 33

<210> SEQ ID NO 25
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 25
atggaaaccg tcgaaaaaac catgaaaatg gac 33

<210> SEQ ID NO 26
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Neisseria gonorrhoea

<400> SEQUENCE: 26
atggaaaccg tcgaaaaaac catgaaaatg gac 33

<210> SEQ ID NO 27

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<211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Neisseria gonorrhoea

 <400> SEQUENCE: 27

 atggaaaccg tcgaaaaaac catgaaaatg gac 33

<210> SEQ ID NO 28
 <211> LENGTH: 32
 <212> TYPE: DNA
 <213> ORGANISM: Neisseria meningitidis

 <400> SEQUENCE: 28

 atggaaaccg tcgaaaaacc atgaccatgg aa 32

<210> SEQ ID NO 29
 <211> LENGTH: 32
 <212> TYPE: DNA
 <213> ORGANISM: Neisseria meningitidis

 <400> SEQUENCE: 29

 atggaaaccg tcgaaaaacc atgaccatgg aa 32

<210> SEQ ID NO 30
 <211> LENGTH: 32
 <212> TYPE: DNA
 <213> ORGANISM: Neisseria meningitidis

 <400> SEQUENCE: 30

 atggaaaccg tcgaaaaacc atgaccatgg aa 32

<210> SEQ ID NO 31
 <211> LENGTH: 390
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

 <400> SEQUENCE: 31

 Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15

 Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Glu Thr Pro
 20 25 30

 Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu
 35 40 45

 Thr Pro Ser Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
 50 55 60

 Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
 65 70 75 80

 Val Lys Met Glu Thr Val Glu Lys Thr Met Thr Met Glu Asp Gly Val
 85 90 95

 Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 100 105 110

 Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 115 120 125

 Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
 130 135 140

 Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
 145 150 155 160

 Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
 165 170 175

-continued

Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
 180 185 190
 Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 195 200 205
 Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 210 215 220
 Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 225 230 235 240
 Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 245 250 255
 Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 260 265 270
 Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 275 280 285
 Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 290 295 300
 Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
 305 310 315 320
 Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn
 325 330 335
 Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 340 345 350
 Ile Met Thr Gln Lys Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala
 355 360 365
 Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala
 370 375 380
 Ser Glu Lys Ser Val Tyr
 385 390

<210> SEQ ID NO 32
 <211> LENGTH: 390
 <212> TYPE: PRT
 <213> ORGANISM: *Neisseria meningitidis*

<400> SEQUENCE: 32

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15
 Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Glu Thr Pro
 20 25 30
 Ala Ala Ala Ala Glu Ala Ala Ser Ala Ala Gln Thr Ala Ala Glu
 35 40 45
 Thr Pro Ser Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
 50 55 60
 Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
 65 70 75 80
 Val Lys Met Glu Thr Val Glu Lys Thr Met Thr Met Glu Asp Gly Val
 85 90 95
 Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 100 105 110
 Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 115 120 125
 Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
 130 135 140
 Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
 145 150 155 160

-continued

Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
 165 170 175
 Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
 180 185 190
 Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 195 200 205
 Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 210 215 220
 Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 225 230 235 240
 Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 245 250 255
 Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 260 265 270
 Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 275 280 285
 Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 290 295 300
 Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
 305 310 315 320
 Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn
 325 330 335
 Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 340 345 350
 Ile Met Thr Gln Lys Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala
 355 360 365
 Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala
 370 375 380
 Ser Glu Lys Ser Val Tyr
 385 390

<210> SEQ ID NO 33

<211> LENGTH: 390

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 33

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15
 Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Glu Thr Pro
 20 25 30
 Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu
 35 40 45
 Thr Pro Ser Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
 50 55 60
 Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
 65 70 75 80
 Val Lys Met Glu Thr Val Glu Lys Thr Met Thr Met Glu Asp Gly Val
 85 90 95
 Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 100 105 110
 Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 115 120 125
 Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln

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130			135			140									
Gly	Gly	Gly	Ala	Ala	Ala	Thr	Phe	Thr	Ala	Pro	Gly	Arg	Thr	Ser	Thr
145					150					155					160
Phe	Ser	Phe	Lys	Ala	Leu	Gln	Pro	Gly	Leu	Tyr	Ile	Tyr	His	Cys	Ala
			165						170					175	
Val	Ala	Pro	Val	Gly	Met	His	Ile	Ala	Asn	Gly	Met	Tyr	Gly	Leu	Ile
			180					185					190		
Leu	Val	Glu	Pro	Lys	Glu	Gly	Leu	Pro	Lys	Val	Asp	Lys	Glu	Phe	Tyr
		195					200				205				
Ile	Val	Gln	Gly	Asp	Phe	Tyr	Thr	Lys	Gly	Lys	Lys	Gly	Ala	Gln	Gly
	210					215					220				
Leu	Gln	Pro	Phe	Asp	Met	Asp	Lys	Ala	Val	Ala	Glu	Gln	Pro	Glu	Tyr
225				230						235				240	
Val	Val	Phe	Asn	Gly	His	Val	Gly	Ala	Ile	Ala	Gly	Asp	Asn	Ala	Leu
			245					250						255	
Lys	Ala	Lys	Ala	Gly	Glu	Thr	Val	Arg	Met	Tyr	Val	Gly	Asn	Gly	Gly
		260						265					270		
Pro	Asn	Leu	Val	Ser	Ser	Phe	His	Val	Ile	Gly	Glu	Ile	Phe	Asp	Lys
		275					280						285		
Val	Tyr	Val	Glu	Gly	Gly	Lys	Leu	Ile	Asn	Glu	Asn	Val	Gln	Ser	Thr
	290						295				300				
Ile	Val	Pro	Ala	Gly	Gly	Ser	Ala	Ile	Val	Glu	Phe	Lys	Val	Asp	Ile
305				310						315				320	
Pro	Gly	Ser	Tyr	Thr	Leu	Val	Asp	His	Ser	Ile	Phe	Arg	Ala	Phe	Asn
			325						330					335	
Lys	Gly	Ala	Leu	Gly	Gln	Leu	Lys	Val	Glu	Gly	Ala	Glu	Asn	Pro	Glu
		340						345					350		
Ile	Ile	Thr	Gln	Lys	Leu	Ser	Asp	Thr	Ala	Tyr	Ala	Gly	Asn	Gly	Ala
		355					360					365			
Ala	Pro	Ala	Ala	Ser	Ala	Pro	Ala	Ala	Ser	Ala	Pro	Ala	Ala	Ser	Ala
	370					375					380				
Ser	Glu	Lys	Ser	Val	Tyr										
385				390											

<210> SEQ ID NO 34

<211> LENGTH: 390

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 34

Met	Lys	Arg	Gln	Ala	Leu	Ala	Ala	Met	Ile	Ala	Ser	Leu	Phe	Ala	Leu
1				5					10					15	
Ala	Ala	Cys	Gly	Gly	Glu	Pro	Ala	Ala	Gln	Ala	Pro	Ala	Glu	Thr	Pro
		20						25					30		
Ala	Ala	Ala	Ala	Glu	Ala	Ala	Ser	Ser	Ala	Ala	Gln	Thr	Ala	Ala	Glu
		35					40					45			
Thr	Pro	Ser	Gly	Glu	Leu	Pro	Val	Ile	Asp	Ala	Val	Thr	Thr	His	Ala
	50					55					60				
Pro	Glu	Val	Pro	Pro	Ala	Ile	Asp	Arg	Asp	Tyr	Pro	Ala	Lys	Val	Arg
65					70					75				80	
Val	Lys	Met	Glu	Thr	Val	Glu	Lys	Thr	Met	Thr	Met	Glu	Asp	Gly	Val
				85					90					95	
Glu	Tyr	Arg	Tyr	Trp	Thr	Phe	Asp	Gly	Asp	Val	Pro	Gly	Arg	Met	Ile
				100				105						110	

-continued

Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 115 120 125
 Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
 130 135 140
 Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
 145 150 155 160
 Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
 165 170 175
 Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
 180 185 190
 Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 195 200 205
 Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 210 215 220
 Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 225 230 235 240
 Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 245 250 255
 Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 260 265 270
 Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 275 280 285
 Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 290 295 300
 Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
 305 310 315 320
 Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn
 325 330 335
 Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 340 345 350
 Ile Met Thr Gln Lys Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala
 355 360 365
 Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala
 370 375 380
 Ser Glu Lys Ser Val Tyr
 385 390

<210> SEQ ID NO 35
 <211> LENGTH: 336
 <212> TYPE: PRT
 <213> ORGANISM: *Neisseria meningitidis*

<400> SEQUENCE: 35

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Ala Pro Ala Glu Thr Pro Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala
 20 25 30
 Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
 35 40 45
 Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
 50 55 60
 Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
 65 70 75 80
 Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp
 85 90 95

-continued

Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
 100 105 110
 Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
 115 120 125
 His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala
 130 135 140
 Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu
 145 150 155 160
 Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn
 165 170 175
 Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
 180 185 190
 Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
 195 200 205
 Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val
 210 215 220
 Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
 225 230 235 240
 Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
 245 250 255
 Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile
 260 265 270
 Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
 275 280 285
 Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
 290 295 300
 Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
 305 310 315 320
 Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330 335

<210> SEQ ID NO 36

<211> LENGTH: 336

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 36

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Ala Pro Ala Glu Thr Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala
 20 25 30
 Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
 35 40 45
 Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
 50 55 60
 Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
 65 70 75 80
 Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly Asp
 85 90 95
 Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
 100 105 110
 Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
 115 120 125
 His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala

-continued

130					135					140					
Pro	Gly	Arg	Thr	Ser	Thr	Phe	Ser	Phe	Lys	Ala	Leu	Gln	Pro	Gly	Leu
145					150					155					160
Tyr	Ile	Tyr	His	Cys	Ala	Val	Ala	Pro	Val	Gly	Met	His	Ile	Ala	Asn
				165					170					175	
Gly	Met	Tyr	Gly	Leu	Ile	Leu	Val	Glu	Pro	Lys	Glu	Gly	Leu	Pro	Lys
			180					185					190		
Val	Asp	Lys	Glu	Phe	Tyr	Ile	Val	Gln	Gly	Asp	Phe	Tyr	Thr	Lys	Gly
		195					200					205			
Lys	Lys	Gly	Ala	Gln	Gly	Leu	Gln	Pro	Phe	Asp	Met	Asp	Lys	Ala	Ile
	210					215					220				
Ala	Glu	Gln	Pro	Glu	Tyr	Val	Val	Phe	Asn	Gly	His	Val	Gly	Ala	Ile
225					230					235					240
Ala	Gly	Asp	Asn	Ala	Leu	Lys	Ala	Lys	Ala	Gly	Glu	Thr	Val	Arg	Met
			245						250					255	
Tyr	Val	Gly	Asn	Gly	Gly	Pro	Asn	Leu	Val	Ser	Ser	Phe	His	Val	Ile
			260					265						270	
Gly	Glu	Ile	Phe	Asp	Lys	Val	Tyr	Val	Glu	Gly	Gly	Lys	Leu	Ile	Asn
		275					280					285			
Glu	Asn	Val	Gln	Ser	Thr	Ile	Val	Pro	Ala	Gly	Gly	Ser	Ala	Ile	Val
	290					295					300				
Glu	Phe	Lys	Val	Asp	Ile	Pro	Gly	Ser	Tyr	Thr	Leu	Val	Asp	His	Ser
305					310					315					320
Ile	Phe	Arg	Ala	Phe	Asn	Lys	Gly	Ala	Leu	Gly	Gln	Leu	Lys	Val	Glu
				325					330					335	

<210> SEQ ID NO 37

<211> LENGTH: 336

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 37

Ala	Ser	Leu	Phe	Ala	Leu	Ala	Ala	Cys	Gly	Gly	Glu	Pro	Ala	Ala	Gln
1				5					10					15	
Ala	Pro	Ala	Glu	Thr	Pro	Ala	Ala	Ala	Ala	Glu	Ala	Ala	Ser	Ser	Ala
		20						25					30		
Ala	Gln	Thr	Ala	Ala	Glu	Thr	Pro	Ser	Gly	Glu	Leu	Pro	Val	Ile	Asp
		35					40						45		
Ala	Val	Thr	Thr	His	Ala	Pro	Glu	Val	Pro	Pro	Ala	Ile	Asp	Arg	Asp
	50					55					60				
Tyr	Pro	Ala	Lys	Val	Arg	Val	Lys	Met	Glu	Thr	Val	Glu	Lys	Thr	Met
65					70					75					80
Thr	Met	Glu	Asp	Gly	Val	Glu	Tyr	Arg	Tyr	Trp	Thr	Phe	Asp	Gly	Asp
			85						90					95	
Val	Pro	Gly	Arg	Met	Ile	Arg	Val	Arg	Glu	Gly	Asp	Thr	Val	Glu	Val
			100						105					110	
Glu	Phe	Ser	Asn	Asn	Pro	Ser	Ser	Thr	Val	Pro	His	Asn	Val	Asp	Phe
		115						120					125		
His	Ala	Ala	Thr	Gly	Gln	Gly	Gly	Gly	Ala	Ala	Ala	Thr	Phe	Thr	Ala
	130							135					140		
Pro	Gly	Arg	Thr	Ser	Thr	Phe	Ser	Phe	Lys	Ala	Leu	Gln	Pro	Gly	Leu
145					150					155					160
Tyr	Ile	Tyr	His	Cys	Ala	Val	Ala	Pro	Val	Gly	Met	His	Ile	Ala	Asn
				165						170					175

-continued

Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
180 185 190

Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
195 200 205

Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val
210 215 220

Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
225 230 235 240

Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
245 250 255

Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile
260 265 270

Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
275 280 285

Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
290 295 300

Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
305 310 315 320

Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
325 330 335

<210> SEQ ID NO 38
 <211> LENGTH: 336
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 38

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Pro Ala Gln
1 5 10 15

Ala Pro Ala Glu Thr Pro Ala Ala Ala Glu Ala Ala Ser Ser Ala
20 25 30

Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
35 40 45

Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
50 55 60

Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
65 70 75 80

Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp
85 90 95

Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
100 105 110

Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
115 120 125

His Ala Ala Thr Gly Gln Gly Gly Ala Ala Ala Thr Phe Thr Ala
130 135 140

Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu
145 150 155 160

Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn
165 170 175

Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
180 185 190

Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
195 200 205

Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val
210 215 220

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Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
 225 230 235 240
 Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
 245 250 255
 Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile
 260 265 270
 Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
 275 280 285
 Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
 290 295 300
 Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
 305 310 315 320
 Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330 335

<210> SEQ ID NO 39
 <211> LENGTH: 336
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 39

Ala Ser Leu Leu Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Ala Pro Ala Glu Thr Pro Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala
 20 25 30
 Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
 35 40 45
 Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
 50 55 60
 Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
 65 70 75 80
 Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp
 85 90 95
 Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
 100 105 110
 Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
 115 120 125
 His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala
 130 135 140
 Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu
 145 150 155 160
 Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn
 165 170 175
 Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
 180 185 190
 Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
 195 200 205
 Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val
 210 215 220
 Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
 225 230 235 240
 Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
 245 250 255
 Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile

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Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
305 310 315 320

Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
325 330 335

<210> SEQ ID NO 41

<211> LENGTH: 336

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 41

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
1 5 10 15

Ala Pro Ala Glu Thr Pro Ala Ala Ala Glu Ala Ala Ser Ser Ala
20 25 30

Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
35 40 45

Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
50 55 60

Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
65 70 75 80

Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp
85 90 95

Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
100 105 110

Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
115 120 125

His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala
130 135 140

Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu
145 150 155 160

Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn
165 170 175

Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
180 185 190

Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
195 200 205

Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val
210 215 220

Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
225 230 235 240

Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
245 250 255

Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile
260 265 270

Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
275 280 285

Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
290 295 300

Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
305 310 315 320

Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
325 330 335

<210> SEQ ID NO 42

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<211> LENGTH: 386
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis
 <400> SEQUENCE: 42

Met Lys Arg Gln Ala Leu Ala Ala Ile Ile Ala Ser Met Phe Ala Leu
 1 5 10 15
 Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Thr Pro Ala Ala Ser Ala
 20 25 30
 Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly
 35 40 45
 Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro
 50 55 60
 Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu
 65 70 75 80
 Thr Val Glu Lys Thr Met Lys Met Asp Asp Gly Val Glu Tyr Arg Tyr
 85 90 95
 Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu
 100 105 110
 Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val
 115 120 125
 Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala
 130 135 140
 Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys
 145 150 155 160
 Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val
 165 170 175
 Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro
 180 185 190
 Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly
 195 200 205
 Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe
 210 215 220
 Asp Met Asp Lys Ala Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn
 225 230 235 240
 Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala
 245 250 255
 Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val
 260 265 270
 Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu
 275 280 285
 Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala
 290 295 300
 Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr
 305 310 315 320
 Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu
 325 330 335
 Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu Ile Met Thr Gln
 340 345 350
 Lys Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala Ala Pro Ala Ala
 355 360 365
 Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Lys Ser
 370 375 380
 Asp Tyr

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385

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<210> SEQ ID NO 43
<211> LENGTH: 332
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 43

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
1           5           10           15
Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Ala Ala
20           25           30
Ala Glu Thr Pro Ala Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
35           40           45
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
50           55           60
Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met Thr Met Glu Asp
65           70           75           80
Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg
85           90           95
Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn
100          105          110
Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr
115          120          125
Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr
130          135          140
Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His
145          150          155          160
Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly
165          170          175
Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu
180          185          190
Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala
195          200          205
Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Ile Ala Glu Gln Pro
210          215          220
Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn
225          230          235          240
Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn
245          250          255
Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe
260          265          270
Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln
275          280          285
Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val
290          295          300
Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala
305          310          315          320
Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
325          330

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<210> SEQ ID NO 44
<211> LENGTH: 332
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

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-continued

<400> SEQUENCE: 44

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Ala Ala
 20 25 30

Ala Glu Thr Pro Ala Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45

His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60

Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp
 65 70 75 80

Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg
 85 90 95

Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn
 100 105 110

Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr
 115 120 125

Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr
 130 135 140

Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His
 145 150 155 160

Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly
 165 170 175

Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu
 180 185 190

Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala
 195 200 205

Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Ile Ala Glu Gln Pro
 210 215 220

Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn
 225 230 235 240

Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn
 245 250 255

Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe
 260 265 270

Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln
 275 280 285

Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val
 290 295 300

Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala
 305 310 315 320

Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330

<210> SEQ ID NO 45

<211> LENGTH: 332

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 45

Ala Ser Met Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Thr Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30

-continued

Ala Glu Thr Pro Ala Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45
 His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp
 65 70 75 80
 Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg
 85 90 95
 Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn
 100 105 110
 Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr
 115 120 125
 Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr
 130 135 140
 Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His
 145 150 155 160
 Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly
 165 170 175
 Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu
 180 185 190
 Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala
 195 200 205
 Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Ile Ala Glu Gln Pro
 210 215 220
 Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn
 225 230 235 240
 Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn
 245 250 255
 Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe
 260 265 270
 Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln
 275 280 285
 Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val
 290 295 300
 Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala
 305 310 315 320
 Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330

<210> SEQ ID NO 46

<211> LENGTH: 332

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 46

Ala Ser Met Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Thr Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30
 Ala Glu Thr Pro Ala Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45
 His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp
 65 70 75 80

-continued

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 48

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Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
1           5           10           15
Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Ala Ser Ala
20           25           30
Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu Thr Pro Thr Gly
35           40           45
Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro
50           55           60
Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu
65           70           75           80
Thr Val Glu Lys Pro
85

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<210> SEQ ID NO 49

<211> LENGTH: 85

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 49

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Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
1           5           10           15
Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Ala Ser Ala
20           25           30
Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu Thr Pro Thr Gly
35           40           45
Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro
50           55           60
Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu
65           70           75           80
Thr Val Glu Lys Pro
85

```

<210> SEQ ID NO 50

<211> LENGTH: 85

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 50

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Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
1           5           10           15
Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Ala Ser Ala
20           25           30
Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu Thr Pro Thr Gly
35           40           45
Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro
50           55           60
Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu
65           70           75           80
Thr Val Glu Lys Pro
85

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<210> SEQ ID NO 51

<211> LENGTH: 75

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

-continued

<400> SEQUENCE: 51

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30

Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45

His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60

Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
 65 70 75

<210> SEQ ID NO 52

<211> LENGTH: 75

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 52

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30

Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45

His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60

Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
 65 70 75

<210> SEQ ID NO 53

<211> LENGTH: 75

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 53

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30

Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45

His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60

Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
 65 70 75

<210> SEQ ID NO 54

<211> LENGTH: 75

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 54

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30

Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr

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      35          40          45
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
  50          55          60
Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
  65          70          75

```

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<210> SEQ ID NO 55
<211> LENGTH: 75
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

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<400> SEQUENCE: 55

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```

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1          5          10          15
Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20          25          30
Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35          40          45
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50          55          60
Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
 65          70          75

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<210> SEQ ID NO 56
<211> LENGTH: 75
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

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<400> SEQUENCE: 56

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```

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1          5          10          15
Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20          25          30
Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35          40          45
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50          55          60
Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
 65          70          75

```

```

<210> SEQ ID NO 57
<211> LENGTH: 75
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

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<400> SEQUENCE: 57

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```

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1          5          10          15
Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20          25          30
Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35          40          45
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50          55          60
Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
 65          70          75

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<210> SEQ ID NO 58

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-continued

<211> LENGTH: 75
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 58

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30
 Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45
 His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
 65 70 75

<210> SEQ ID NO 59
 <211> LENGTH: 75
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 59

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Pro Ala Gln
 1 5 10 15
 Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30
 Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45
 His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Pro
 65 70 75

<210> SEQ ID NO 60
 <211> LENGTH: 96
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 60

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30
 Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45
 His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Pro Arg Pro Trp Lys Thr
 65 70 75 80
 Val Trp Asn Thr Ala Thr Gly His Leu Thr Ala Thr Phe Arg Val Ala
 85 90 95

<210> SEQ ID NO 61
 <211> LENGTH: 337
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 61

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro

-continued

1	5	10	15
Ala Glu Thr	Pro Ala Ala Thr	Ala Ser Ala Glu Ala	Pro Ala Ala Ser
	20	25	30
Asn Ser Gln	Ala Ala Ala Glu Thr	Pro Ser Ser Glu Leu	Pro Val Ile
	35	40	45
Asp Ala Ile	Val Thr His Ala Pro	Glu Val Pro Pro	Pro Thr Asp Arg
	50	55	60
Asp His Pro	Ala Lys Val Arg Val	Lys Met Glu Thr Val	Glu Lys Thr
	65	70	75
Met Lys Met	Asp Asp Gly Val Glu	Tyr His Tyr Trp Thr	Phe Asp Gly
	85	90	95
Asp Val Pro	Gly Arg Met Ile Arg	Val Arg Glu Gly Asp	Thr Val Glu
	100	105	110
Val Glu Phe	Ser Asn Asn Pro Ser	Ser Thr Val Pro His	Asn Val Asp
	115	120	125
Phe His Ala	Ala Thr Gly Gln Gly	Gly Gly Ala Ala Ala	Thr Phe Thr
	130	135	140
Ala Pro Gly	Arg Thr Ser Thr Phe	Ser Phe Lys Ala Leu	Gln Ala Gly
	145	150	155
Leu Tyr Ile	Tyr His Cys Ala Val	Ala Pro Val Gly Met	His Ile Ala
	165	170	175
Asn Gly Met	Tyr Gly Leu Ile Leu	Val Glu Pro Lys Glu	Gly Leu Pro
	180	185	190
Lys Val Asp	Lys Glu Phe Tyr Ile	Val Gln Gly Asp Phe	Tyr Thr Lys
	195	200	205
Gly Lys Lys	Gly Ala Gln Gly Leu	Gln Pro Phe Asp Met	Asp Lys Ala
	210	215	220
Ile Ala Glu	Gln Pro Glu Tyr Val	Val Phe Asn Gly His	Val Gly Ser
	225	230	235
Ile Ala Gly	Asp Asn Ala Leu Lys	Ala Lys Ala Gly Glu	Thr Ile Arg
	245	250	255
Met Tyr Val	Gly Asn Gly Gly Pro	Asn Leu Val Ser Ser	Phe His Val
	260	265	270
Ile Gly Glu	Ile Phe Asp Lys Val	Tyr Val Glu Gly Gly	Lys Leu Ile
	275	280	285
Asn Glu Asn	Val Gln Ser Thr Ile	Val Pro Ala Gly Gly	Ser Ala Ile
	290	295	300
Val Glu Phe	Lys Val Asp Ile Pro	Gly Ser Tyr Thr Leu	Val Asp His
	305	310	315
Ser Ile Phe	Arg Ala Phe Asn Lys	Gly Ala Leu Gly Gln	Leu Lys Val
	325	330	335

Glu

<210> SEQ ID NO 62

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 62

Ala Ser Val	Phe Ala Leu Ala Ala	Cys Gly Glu Gln Ala	Ala Lys Pro
	5	10	15
Ala Glu Thr	Pro Ala Ala Thr	Ala Ser Ala Glu Ala	Pro Ala Ala Ser
	20	25	30
Asn Ser Gln	Ala Ala Ala Glu Thr	Pro Ser Ser Glu Leu	Pro Val Ile

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65          70          75          80
Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
      85          90          95
Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
      100          105          110
Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
      115          120          125
Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
      130          135          140
Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
      145          150          155          160
Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
      165          170          175
Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
      180          185          190
Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
      195          200          205
Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
      210          215          220
Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
      225          230          235          240
Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
      245          250          255
Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
      260          265          270
Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
      275          280          285
Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
      290          295          300
Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
      305          310          315          320
Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
      325          330          335

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Glu

<210> SEQ ID NO 64

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 64

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Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
1          5          10          15
Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
20          25          30
Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
35          40          45
Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
50          55          60
Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
65          70          75          80
Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
85          90          95
Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu

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100					105					110					
Val	Glu	Phe	Ser	Asn	Asn	Pro	Ser	Ser	Thr	Val	Pro	His	Asn	Val	Asp
	115					120					125				
Phe	His	Ala	Ala	Thr	Gly	Gln	Gly	Gly	Gly	Ala	Ala	Ala	Thr	Phe	Thr
	130					135					140				
Ala	Pro	Gly	Arg	Thr	Ser	Thr	Phe	Ser	Phe	Lys	Ala	Leu	Gln	Ala	Gly
	145					150					155				160
Leu	Tyr	Ile	Tyr	His	Cys	Ala	Val	Ala	Pro	Val	Gly	Met	His	Ile	Ala
				165					170					175	
Asn	Gly	Met	Tyr	Gly	Leu	Ile	Leu	Val	Glu	Pro	Lys	Glu	Gly	Leu	Pro
			180					185						190	
Lys	Val	Asp	Lys	Glu	Phe	Tyr	Ile	Val	Gln	Gly	Asp	Phe	Tyr	Thr	Lys
		195					200					205			
Gly	Lys	Lys	Gly	Ala	Gln	Gly	Leu	Gln	Pro	Phe	Asp	Met	Asp	Lys	Ala
	210					215					220				
Ile	Ala	Glu	Gln	Pro	Glu	Tyr	Val	Val	Phe	Asn	Gly	His	Val	Gly	Ser
	225					230					235				240
Ile	Ala	Gly	Asp	Asn	Ala	Leu	Lys	Ala	Lys	Ala	Gly	Glu	Thr	Ile	Arg
				245					250					255	
Met	Tyr	Val	Gly	Asn	Gly	Gly	Pro	Asn	Leu	Val	Ser	Ser	Phe	His	Val
			260					265						270	
Ile	Gly	Glu	Ile	Phe	Asp	Lys	Val	Tyr	Val	Glu	Gly	Gly	Lys	Leu	Ile
		275					280						285		
Asn	Glu	Asn	Val	Gln	Ser	Thr	Ile	Val	Pro	Ala	Gly	Gly	Ser	Ala	Ile
	290						295				300				
Val	Glu	Phe	Lys	Val	Asp	Ile	Pro	Gly	Ser	Tyr	Thr	Leu	Val	Asp	His
	305					310					315				320
Ser	Ile	Phe	Arg	Ala	Phe	Asn	Lys	Gly	Ala	Leu	Gly	Gln	Leu	Lys	Val
				325					330					335	

Glu

<210> SEQ ID NO 65

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 65

Ala	Ser	Val	Phe	Ala	Leu	Ala	Ala	Cys	Gly	Glu	Gln	Ala	Ala	Lys	Pro
1				5					10					15	
Ala	Glu	Thr	Pro	Ala	Ala	Thr	Ala	Ser	Ala	Glu	Ala	Pro	Ala	Ala	Ser
			20					25					30		
Asn	Ser	Gln	Ala	Ala	Ala	Glu	Thr	Pro	Ser	Ser	Glu	Leu	Pro	Val	Ile
		35					40					45			
Asp	Ala	Ile	Val	Thr	His	Ala	Pro	Glu	Val	Pro	Pro	Pro	Thr	Asp	Arg
	50					55					60				
Asp	His	Pro	Ala	Lys	Val	Arg	Val	Lys	Met	Glu	Thr	Val	Glu	Lys	Thr
	65					70					75			80	
Met	Lys	Met	Asp	Asp	Gly	Val	Glu	Tyr	His	Tyr	Trp	Thr	Phe	Asp	Gly
				85					90					95	
Asp	Val	Pro	Gly	Arg	Met	Ile	Arg	Val	Arg	Glu	Gly	Asp	Thr	Val	Glu
			100					105						110	
Val	Glu	Phe	Ser	Asn	Asn	Pro	Ser	Ser	Thr	Val	Pro	His	Asn	Val	Asp
		115					120					125			
Phe	His	Ala	Ala	Thr	Gly	Gln	Gly	Gly	Gly	Ala	Ala	Ala	Thr	Phe	Thr

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130	135	140
Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly		
145	150	155 160
Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala		
	165	170 175
Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro		
	180	185 190
Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys		
	195	200 205
Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala		
	210	215 220
Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser		
	225	230 235 240
Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg		
	245	250 255
Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val		
	260	265 270
Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile		
	275	280 285
Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile		
	290	295 300
Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His		
	305	310 315 320
Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val		
	325	330 335

Glu

<210> SEQ ID NO 66

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 66

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro		
1	5	10 15
Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser		
	20	25 30
Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile		
	35	40 45
Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg		
	50	55 60
Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr		
	65	70 75 80
Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly		
	85	90 95
Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu		
	100	105 110
Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp		
	115	120 125
Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Thr Phe Thr		
	130	135 140
Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly		
	145	150 155 160
Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala		

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	165		170		175
Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro	180		185		190
Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys	195		200		205
Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala	210		215		220
Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser	225		230		235
Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg	245		250		255
Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val	260		265		270
Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile	275		280		285
Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile	290		295		300
Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His	305		310		315
Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val	325		330		335

Glu

<210> SEQ ID NO 67
 <211> LENGTH: 337
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 67

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro	1		5		10		15
Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser	20		25		30		35
Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile	35		40		45		50
Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg	50		55		60		65
Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr	65		70		75		80
Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly	85		90		95		100
Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu	100		105		110		115
Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp	115		120		125		130
Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr	130		135		140		145
Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly	145		150		155		160
Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala	165		170		175		180
Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro	180		185		190		195
Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys							

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      260          265          270
Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
      275          280          285
Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
      290          295          300
Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
      305          310          315          320
Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
      325          330          335

Glu

<210> SEQ ID NO 70
<211> LENGTH: 337
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 70
Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1          5          10          15
Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20          25          30
Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35          40          45
Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50          55          60
Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65          70          75          80
Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85          90          95
Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
100          105          110
Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
115          120          125
Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
130          135          140
Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
145          150          155          160
Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
165          170          175
Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
180          185          190
Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
195          200          205
Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
210          215          220
Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
225          230          235          240
Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
245          250          255
Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
260          265          270
Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
      275          280          285
Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile

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325 330 335

Glu

<210> SEQ ID NO 72
 <211> LENGTH: 390
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 72

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15

Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Glu Thr Pro
 20 25 30

Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu
 35 40 45

Thr Pro Ser Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
 50 55 60

Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
 65 70 75 80

Val Lys Met Glu Thr Val Glu Lys Thr Met Thr Met Glu Asp Gly Val
 85 90 95

Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 100 105 110

Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 115 120 125

Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
 130 135 140

Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
 145 150 155 160

Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
 165 170 175

Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
 180 185 190

Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 195 200 205

Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 210 215 220

Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 225 230 235 240

Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 245 250 255

Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 260 265 270

Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 275 280 285

Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 290 295 300

Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
 305 310 315 320

Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn
 325 330 335

Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 340 345 350

Ile Met Thr Gln Lys Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala

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Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 340 345 350

Ile Met Thr Gln Lys Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala
 355 360 365

Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala
 370 375 380

Ser Glu Lys Ser Val Tyr
 385 390

<210> SEQ ID NO 74
 <211> LENGTH: 390
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 74

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15

Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Glu Thr Pro
 20 25 30

Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu
 35 40 45

Thr Pro Ser Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
 50 55 60

Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
 65 70 75 80

Val Lys Met Glu Thr Val Glu Lys Thr Met Thr Met Glu Asp Gly Val
 85 90 95

Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 100 105 110

Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 115 120 125

Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
 130 135 140

Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
 145 150 155 160

Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
 165 170 175

Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
 180 185 190

Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 195 200 205

Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 210 215 220

Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 225 230 235 240

Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 245 250 255

Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 260 265 270

Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 275 280 285

Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr
 290 295 300

Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile
 305 310 315 320

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Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn
 325 330 335
 Lys Gly Ala Leu Gly Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu
 340 345 350
 Ile Ile Thr Gln Lys Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala
 355 360 365
 Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala
 370 375 380
 Ser Glu Lys Ser Val Tyr
 385 390

<210> SEQ ID NO 75
 <211> LENGTH: 390
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 75

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15
 Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Glu Thr Pro
 20 25 30
 Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu
 35 40 45
 Thr Pro Ser Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala
 50 55 60
 Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg
 65 70 75 80
 Val Lys Met Glu Thr Val Glu Lys Thr Met Thr Met Glu Asp Gly Val
 85 90 95
 Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile
 100 105 110
 Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro
 115 120 125
 Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly Gln
 130 135 140
 Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr
 145 150 155 160
 Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala
 165 170 175
 Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile
 180 185 190
 Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr
 195 200 205
 Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly
 210 215 220
 Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr
 225 230 235 240
 Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu
 245 250 255
 Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly
 260 265 270
 Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys
 275 280 285
 Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr

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Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
 275 280 285

Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
 290 295 300

Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
 305 310 315 320

Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330 335

<210> SEQ ID NO 77
 <211> LENGTH: 336
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 77

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Glu Thr Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala
 20 25 30

Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
 35 40 45

Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
 50 55 60

Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
 65 70 75 80

Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly Asp
 85 90 95

Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
 100 105 110

Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
 115 120 125

His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala
 130 135 140

Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu
 145 150 155 160

Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn
 165 170 175

Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
 180 185 190

Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
 195 200 205

Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Ile
 210 215 220

Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
 225 230 235 240

Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
 245 250 255

Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile
 260 265 270

Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
 275 280 285

Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
 290 295 300

Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
 305 310 315 320

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Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330 335

<210> SEQ ID NO 78

<211> LENGTH: 336

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 78

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Glu Thr Pro Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala
 20 25 30

Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
 35 40 45

Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
 50 55 60

Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
 65 70 75 80

Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp
 85 90 95

Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
 100 105 110

Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
 115 120 125

His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Thr Phe Thr Ala
 130 135 140

Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu
 145 150 155 160

Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn
 165 170 175

Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
 180 185 190

Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
 195 200 205

Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val
 210 215 220

Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
 225 230 235 240

Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
 245 250 255

Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile
 260 265 270

Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
 275 280 285

Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
 290 295 300

Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
 305 310 315 320

Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330 335

<210> SEQ ID NO 79

<211> LENGTH: 336

<212> TYPE: PRT

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<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 79

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Pro Ala Gln
 1 5 10 15

Ala Pro Ala Glu Thr Pro Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala
 20 25 30

Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
 35 40 45

Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
 50 55 60

Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
 65 70 75 80

Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp
 85 90 95

Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
 100 105 110

Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
 115 120 125

His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala
 130 135 140

Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu
 145 150 155 160

Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn
 165 170 175

Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
 180 185 190

Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
 195 200 205

Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val
 210 215 220

Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
 225 230 235 240

Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
 245 250 255

Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile
 260 265 270

Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
 275 280 285

Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
 290 295 300

Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
 305 310 315 320

Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330 335

<210> SEQ ID NO 80

<211> LENGTH: 336

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 80

Ala Ser Leu Leu Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Glu Thr Pro Ala Ala Ala Ala Glu Ala Ala Ser Ser Ala

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20				25				30							
Ala	Gln	Thr	Ala	Ala	Glu	Thr	Pro	Ser	Gly	Glu	Leu	Pro	Val	Ile	Asp
	35						40					45			
Ala	Val	Thr	Thr	His	Ala	Pro	Glu	Val	Pro	Pro	Ala	Ile	Asp	Arg	Asp
	50					55					60				
Tyr	Pro	Ala	Lys	Val	Arg	Val	Lys	Met	Glu	Thr	Val	Glu	Lys	Thr	Met
	65				70					75					80
Thr	Met	Glu	Asp	Gly	Val	Glu	Tyr	Arg	Tyr	Trp	Thr	Phe	Asp	Gly	Asp
			85						90					95	
Val	Pro	Gly	Arg	Met	Ile	Arg	Val	Arg	Glu	Gly	Asp	Thr	Val	Glu	Val
			100						105					110	
Glu	Phe	Ser	Asn	Asn	Pro	Ser	Ser	Thr	Val	Pro	His	Asn	Val	Asp	Phe
		115					120					125			
His	Ala	Ala	Thr	Gly	Gln	Gly	Gly	Gly	Ala	Ala	Ala	Thr	Phe	Thr	Ala
	130					135					140				
Pro	Gly	Arg	Thr	Ser	Thr	Phe	Ser	Phe	Lys	Ala	Leu	Gln	Pro	Gly	Leu
	145				150					155					160
Tyr	Ile	Tyr	His	Cys	Ala	Val	Ala	Pro	Val	Gly	Met	His	Ile	Ala	Asn
			165						170					175	
Gly	Met	Tyr	Gly	Leu	Ile	Leu	Val	Glu	Pro	Lys	Glu	Gly	Leu	Pro	Lys
		180							185				190		
Val	Asp	Lys	Glu	Phe	Tyr	Ile	Val	Gln	Gly	Asp	Phe	Tyr	Thr	Lys	Gly
	195					200						205			
Lys	Lys	Gly	Ala	Gln	Gly	Leu	Gln	Pro	Phe	Asp	Met	Asp	Lys	Ala	Val
	210					215					220				
Ala	Glu	Gln	Pro	Glu	Tyr	Val	Val	Phe	Asn	Gly	His	Val	Gly	Ala	Ile
	225				230					235					240
Ala	Gly	Asp	Asn	Ala	Leu	Lys	Ala	Lys	Ala	Gly	Glu	Thr	Val	Arg	Met
			245						250					255	
Tyr	Val	Gly	Asn	Gly	Gly	Pro	Asn	Leu	Val	Ser	Ser	Phe	His	Val	Ile
		260					265						270		
Gly	Glu	Ile	Phe	Asp	Lys	Val	Tyr	Val	Glu	Gly	Gly	Lys	Leu	Ile	Asn
		275				280						285			
Glu	Asn	Val	Gln	Ser	Thr	Ile	Val	Pro	Ala	Gly	Gly	Ser	Ala	Ile	Val
	290					295					300				
Glu	Phe	Lys	Val	Asp	Ile	Pro	Gly	Ser	Tyr	Thr	Leu	Val	Asp	His	Ser
	305				310					315					320
Ile	Phe	Arg	Ala	Phe	Asn	Lys	Gly	Ala	Leu	Gly	Gln	Leu	Lys	Val	Glu
			325						330					335	

<210> SEQ ID NO 81

<211> LENGTH: 336

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 81

Ala	Ser	Leu	Leu	Ala	Leu	Ala	Ala	Cys	Gly	Gly	Glu	Pro	Ala	Ala	Gln
	1				5				10				15		
Ala	Pro	Ala	Glu	Thr	Pro	Ala	Ala	Ala	Ala	Glu	Ala	Ala	Ser	Ser	Ala
		20					25						30		
Ala	Gln	Thr	Ala	Ala	Glu	Thr	Pro	Ser	Gly	Glu	Leu	Pro	Val	Ile	Asp
		35					40						45		
Ala	Val	Thr	Thr	His	Ala	Pro	Glu	Val	Pro	Pro	Ala	Ile	Asp	Arg	Asp
		50				55					60				

-continued

Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
 65 70 75 80
 Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp
 85 90 95
 Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
 100 105 110
 Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe
 115 120 125
 His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala
 130 135 140
 Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu
 145 150 155 160
 Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn
 165 170 175
 Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys
 180 185 190
 Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly
 195 200 205
 Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val
 210 215 220
 Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile
 225 230 235 240
 Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met
 245 250 255
 Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile
 260 265 270
 Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn
 275 280 285
 Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val
 290 295 300
 Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser
 305 310 315 320
 Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330 335

<210> SEQ ID NO 82

<211> LENGTH: 336

<212> TYPE: PRT

<213> ORGANISM: *Neisseria meningitidis*

<400> SEQUENCE: 82

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Ala Pro Ala Glu Thr Pro Ala Ala Ala Glu Ala Ala Ser Ser Ala
 20 25 30
 Ala Gln Thr Ala Ala Glu Thr Pro Ser Gly Glu Leu Pro Val Ile Asp
 35 40 45
 Ala Val Thr Thr His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp
 50 55 60
 Tyr Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met
 65 70 75 80
 Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp
 85 90 95
 Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val
 100 105 110

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Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr
 130 135 140
 Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His
 145 150 155 160
 Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly
 165 170 175
 Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu
 180 185 190
 Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala
 195 200 205
 Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Ile Ala Glu Gln Pro
 210 215 220
 Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn
 225 230 235 240
 Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn
 245 250 255
 Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe
 260 265 270
 Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln
 275 280 285
 Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val
 290 295 300
 Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala
 305 310 315 320
 Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330

<210> SEQ ID NO 85
 <211> LENGTH: 332
 <212> TYPE: PRT
 <213> ORGANISM: *Neisseria meningitidis*

<400> SEQUENCE: 85

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Ala Ala
 20 25 30
 Ala Glu Thr Pro Ala Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45
 His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp
 65 70 75 80
 Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg
 85 90 95
 Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn
 100 105 110
 Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr
 115 120 125
 Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr
 130 135 140
 Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His
 145 150 155 160
 Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly
 165 170 175

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Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu
 180 185 190
 Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala
 195 200 205
 Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Ile Ala Glu Gln Pro
 210 215 220
 Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn
 225 230 235 240
 Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn
 245 250 255
 Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe
 260 265 270
 Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln
 275 280 285
 Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val
 290 295 300
 Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala
 305 310 315 320
 Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330

<210> SEQ ID NO 86

<211> LENGTH: 332

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 86

Ala Ser Met Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Thr Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30
 Ala Glu Thr Pro Ala Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45
 His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp
 65 70 75 80
 Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg
 85 90 95
 Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn
 100 105 110
 Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr
 115 120 125
 Gly Gln Gly Gly Glu Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr
 130 135 140
 Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His
 145 150 155 160
 Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly
 165 170 175
 Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu
 180 185 190
 Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala
 195 200 205
 Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Ile Ala Glu Gln Pro

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210	215	220
Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn 225 230 235 240		
Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn 245 250 255		
Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe 260 265 270		
Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln 275 280 285		
Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val 290 295 300		
Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala 305 310 315 320		
Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu 325 330		

<210> SEQ ID NO 87

<211> LENGTH: 332

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 87

Ala Ser Met Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln 1 5 10 15		
Thr Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala 20 25 30		
Ala Glu Thr Pro Ala Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr 35 40 45		
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys 50 55 60		
Val Arg Val Lys Met Glu Thr Val Glu Lys Thr Met Lys Met Asp Asp 65 70 75 80		
Gly Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg 85 90 95		
Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn 100 105 110		
Asn Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr 115 120 125		
Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr 130 135 140		
Ser Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His 145 150 155 160		
Cys Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly 165 170 175		
Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu 180 185 190		
Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala 195 200 205		
Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Ile Ala Glu Gln Pro 210 215 220		
Glu Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn 225 230 235 240		
Ala Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn 245 250 255		

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Gly Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe
 260 265 270

Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln
 275 280 285

Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val
 290 295 300

Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala
 305 310 315 320

Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330

<210> SEQ ID NO 88
 <211> LENGTH: 385
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 88

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15

Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Ala Ser Ala
 20 25 30

Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu Thr Pro Thr Gly
 35 40 45

Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro
 50 55 60

Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu
 65 70 75 80

Thr Val Glu Lys Met Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp
 85 90 95

Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly
 100 105 110

Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro
 115 120 125

His Asn Val Asp Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala
 130 135 140

Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala
 145 150 155 160

Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly
 165 170 175

Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys
 180 185 190

Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp
 195 200 205

Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp
 210 215 220

Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly
 225 230 235 240

His Val Gly Ser Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly
 245 250 255

Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser
 260 265 270

Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly
 275 280 285

Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly
 290 295 300

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Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr
 305 310 315 320
 Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly
 325 330 335
 Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu Ile Met Thr Gln Lys
 340 345 350
 Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala Ala Pro Ala Ala Ser
 355 360 365
 Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Ser Glu Lys Ser Val
 370 375 380
 Tyr
 385

<210> SEQ ID NO 89
 <211> LENGTH: 385
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 89

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15
 Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Ala Ser Ala
 20 25 30
 Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu Thr Pro Thr Gly
 35 40 45
 Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro
 50 55 60
 Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu
 65 70 75 80
 Thr Val Glu Lys Met Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp
 85 90 95
 Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly
 100 105 110
 Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro
 115 120 125
 His Asn Val Asp Phe His Ala Ala Thr Gly Gln Gly Gly Ala Ala
 130 135 140
 Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala
 145 150 155 160
 Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly
 165 170 175
 Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys
 180 185 190
 Glu Gly Leu Pro Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp
 195 200 205
 Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly Pro Gln Pro Phe Asp
 210 215 220
 Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly
 225 230 235 240
 His Val Gly Ala Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly
 245 250 255
 Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser
 260 265 270
 Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly

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Glu Thr Val Arg Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser
 260 265 270
 Ser Phe His Val Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly
 275 280 285
 Gly Lys Leu Ile Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly
 290 295 300
 Gly Ser Ala Ile Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr
 305 310 315 320
 Leu Val Asp His Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly
 325 330 335
 Gln Leu Lys Val Glu Gly Ala Glu Asn Pro Glu Ile Met Thr Gln Lys
 340 345 350
 Leu Ser Asp Thr Ala Tyr Ala Gly Asn Gly Ala Ala Pro Ala Ala Ser
 355 360 365
 Ala Pro Ala Ala Ser Ala Pro Ala Ala Ser Ala Ser Glu Lys Ser Val
 370 375 380
 Tyr
 385

<210> SEQ ID NO 91
 <211> LENGTH: 385
 <212> TYPE: PRT
 <213> ORGANISM: *Neisseria meningitidis*

<400> SEQUENCE: 91

Met Lys Arg Gln Ala Leu Ala Ala Met Ile Ala Ser Leu Phe Ala Leu
 1 5 10 15
 Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln Ala Pro Ala Ala Ser Ala
 20 25 30
 Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala Ala Glu Thr Pro Thr Gly
 35 40 45
 Glu Leu Pro Val Ile Asp Ala Val Thr Thr His Ala Pro Glu Val Pro
 50 55 60
 Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys Val Arg Val Lys Met Glu
 65 70 75 80
 Thr Val Glu Lys Met Thr Met Glu Asp Gly Val Glu Tyr Arg Tyr Trp
 85 90 95
 Thr Phe Asp Gly Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly
 100 105 110
 Asp Thr Val Glu Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro
 115 120 125
 His Asn Val Asp Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala
 130 135 140
 Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala
 145 150 155 160
 Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly
 165 170 175
 Met His Ile Ala Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys
 180 185 190
 Glu Gly Leu Pro Lys Val Asp Lys Glu Ser Tyr Ile Val Gln Gly Asp
 195 200 205
 Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp
 210 215 220
 Met Asp Lys Ala Val Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly
 225 230 235 240

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210	215	220
Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala 225 230 235 240		
Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly 245 250 255		
Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp 260 265 270		
Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser 275 280 285		
Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp 290 295 300		
Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Asn 305 310 315 320		
Phe Lys Gly Ala Leu Gly Gln Leu Lys Val Glu 325 330		

<210> SEQ ID NO 93

<211> LENGTH: 331

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 93

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln 1 5 10 15		
Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala 20 25 30		
Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr 35 40 45		
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys 50 55 60		
Val Arg Val Lys Met Glu Thr Val Glu Lys Met Thr Met Glu Asp Gly 65 70 75 80		
Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met 85 90 95		
Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn 100 105 110		
Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly 115 120 125		
Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser 130 135 140		
Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys 145 150 155 160		
Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu 165 170 175		
Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Ser 180 185 190		
Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln 195 200 205		
Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu 210 215 220		
Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala 225 230 235 240		
Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly 245 250 255		

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Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp
 260 265 270

Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser
 275 280 285

Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp
 290 295 300

Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe
 305 310 315 320

Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330

<210> SEQ ID NO 94
 <211> LENGTH: 331
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 94

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15

Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30

Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45

His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60

Val Arg Val Lys Met Glu Thr Val Glu Lys Met Thr Met Glu Asp Gly
 65 70 75 80

Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met
 85 90 95

Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn
 100 105 110

Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly
 115 120 125

Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser
 130 135 140

Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys
 145 150 155 160

Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu
 165 170 175

Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe
 180 185 190

Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln
 195 200 205

Gly Pro Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu
 210 215 220

Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala
 225 230 235 240

Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly
 245 250 255

Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp
 260 265 270

Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser
 275 280 285

Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp
 290 295 300

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Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe
305 310 315 320

Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
325 330

<210> SEQ ID NO 95

<211> LENGTH: 331

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 95

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
1 5 10 15

Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
20 25 30

Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
35 40 45

His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
50 55 60

Val Arg Val Lys Met Glu Thr Val Glu Lys Met Thr Met Glu Asp Gly
65 70 75 80

Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met
85 90 95

Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn
100 105 110

Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly
115 120 125

Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser
130 135 140

Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys
145 150 155 160

Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu
165 170 175

Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Ser
180 185 190

Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln
195 200 205

Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu
210 215 220

Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala
225 230 235 240

Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly
245 250 255

Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp
260 265 270

Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser
275 280 285

Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp
290 295 300

Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe
305 310 315 320

Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
325 330

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<210> SEQ ID NO 96
<211> LENGTH: 331
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 96

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1           5           10          15
Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20          25          30
Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35          40          45
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50          55          60
Val Arg Val Lys Met Glu Thr Val Glu Lys Met Thr Met Glu Asp Gly
 65          70          75          80
Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met
 85          90          95
Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn
 100         105         110
Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly
 115         120         125
Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser
 130         135         140
Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys
 145         150         155         160
Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu
 165         170         175
Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Ser
 180         185         190
Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln
 195         200         205
Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu
 210         215         220
Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala
 225         230         235         240
Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly
 245         250         255
Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp
 260         265         270
Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser
 275         280         285
Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp
 290         295         300
Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe
 305         310         315         320
Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325         330

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<210> SEQ ID NO 97
<211> LENGTH: 331
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 97

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Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln

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1	5	10	15
Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala	20	25	30
Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr	35	40	45
His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys	50	55	60
Val Arg Val Lys Met Glu Thr Val Glu Lys Met Thr Met Glu Asp Gly	65	70	75
Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met	85	90	95
Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn	100	105	110
Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly	115	120	125
Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser	130	135	140
Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys	145	150	155
Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu	165	170	175
Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Ser	180	185	190
Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln	195	200	205
Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu	210	215	220
Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala	225	230	235
Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly	245	250	255
Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp	260	265	270
Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser	275	280	285
Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp	290	295	300
Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe	305	310	315
Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu	325	330	

<210> SEQ ID NO 98

<211> LENGTH: 331

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 98

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln	1	5	10	15
Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala	20	25	30	
Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr	35	40	45	

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His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Met Thr Met Glu Asp Gly
 65 70 75 80
 Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met
 85 90 95
 Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn
 100 105 110
 Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly
 115 120 125
 Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser
 130 135 140
 Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys
 145 150 155 160
 Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu
 165 170 175
 Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Phe
 180 185 190
 Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln
 195 200 205
 Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu
 210 215 220
 Tyr Val Val Phe Asn Gly His Val Gly Ser Ile Ala Gly Asp Asn Ala
 225 230 235 240
 Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly
 245 250 255
 Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp
 260 265 270
 Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser
 275 280 285
 Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp
 290 295 300
 Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe
 305 310 315 320
 Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330

<210> SEQ ID NO 99

<211> LENGTH: 331

<212> TYPE: PRT

<213> ORGANISM: *Neisseria meningitidis*

<400> SEQUENCE: 99

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Ala Ala Gln
 1 5 10 15
 Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30
 Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45
 His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60
 Val Arg Val Lys Met Glu Thr Val Glu Lys Met Thr Met Glu Asp Gly
 65 70 75 80
 Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met
 85 90 95

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Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn
 100 105 110

Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly
 115 120 125

Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser
 130 135 140

Thr Phe Ser Phe Lys Ala Leu Gln Pro Gly Leu Tyr Ile Tyr His Cys
 145 150 155 160

Ala Val Ala Pro Val Gly Met His Ile Ala Asn Gly Met Tyr Gly Leu
 165 170 175

Ile Leu Val Glu Pro Lys Glu Gly Pro Pro Lys Val Asp Lys Glu Phe
 180 185 190

Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln
 195 200 205

Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu
 210 215 220

Tyr Val Val Phe Asn Gly His Val Gly Ser Ile Ala Gly Asp Asn Ala
 225 230 235 240

Leu Lys Glu Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly
 245 250 255

Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp
 260 265 270

Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser
 275 280 285

Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp
 290 295 300

Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe
 305 310 315 320

Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
 325 330

<210> SEQ ID NO 100

<211> LENGTH: 331

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 100

Ala Ser Leu Phe Ala Leu Ala Ala Cys Gly Gly Glu Pro Pro Ala Gln
 1 5 10 15

Ala Pro Ala Ala Ser Ala Glu Ala Ala Ser Ser Ala Ala Gln Thr Ala
 20 25 30

Ala Glu Thr Pro Thr Gly Glu Leu Pro Val Ile Asp Ala Val Thr Thr
 35 40 45

His Ala Pro Glu Val Pro Pro Ala Ile Asp Arg Asp Tyr Pro Ala Lys
 50 55 60

Val Arg Val Lys Met Glu Thr Val Glu Lys Met Thr Met Glu Asp Gly
 65 70 75 80

Val Glu Tyr Arg Tyr Trp Thr Phe Asp Gly Asp Val Pro Gly Arg Met
 85 90 95

Ile Arg Val Arg Glu Gly Asp Thr Val Glu Val Glu Phe Ser Asn Asn
 100 105 110

Pro Ser Ser Thr Val Pro His Asn Val Asp Phe His Ala Ala Thr Gly
 115 120 125

Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr Ala Pro Gly Arg Thr Ser

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130				135				140							
Thr	Phe	Ser	Phe	Lys	Ala	Leu	Gln	Pro	Gly	Leu	Tyr	Ile	Tyr	His	Cys
145					150					155					160
Ala	Val	Ala	Pro	Val	Gly	Met	His	Ile	Ala	Asn	Gly	Met	Tyr	Gly	Leu
				165					170					175	
Ile	Leu	Val	Glu	Pro	Lys	Glu	Gly	Leu	Pro	Lys	Val	Asp	Lys	Glu	Ser
			180					185					190		
Tyr	Ile	Val	Gln	Gly	Asp	Phe	Tyr	Thr	Lys	Gly	Lys	Lys	Gly	Ala	Gln
		195					200					205			
Gly	Leu	Gln	Pro	Phe	Asp	Met	Asp	Lys	Ala	Val	Ala	Glu	Gln	Pro	Glu
	210				215						220				
Tyr	Val	Val	Phe	Asn	Gly	His	Val	Gly	Ala	Ile	Ala	Gly	Asp	Asn	Ala
225				230						235					240
Leu	Lys	Ala	Lys	Ala	Gly	Glu	Thr	Val	Arg	Met	Tyr	Val	Gly	Asn	Gly
			245						250					255	
Gly	Pro	Asn	Leu	Val	Ser	Ser	Phe	His	Val	Ile	Gly	Glu	Ile	Phe	Asp
		260						265					270		
Lys	Val	Tyr	Val	Glu	Gly	Gly	Lys	Leu	Ile	Asn	Glu	Asn	Val	Gln	Ser
	275						280					285			
Thr	Ile	Val	Pro	Ala	Gly	Gly	Ser	Ala	Ile	Val	Glu	Phe	Lys	Val	Asp
	290					295					300				
Ile	Pro	Gly	Ser	Tyr	Thr	Leu	Val	Asp	His	Ser	Ile	Phe	Arg	Ala	Phe
305				310						315					320
Asn	Lys	Gly	Ala	Leu	Gly	Gln	Leu	Lys	Val	Glu					
			325						330						

<210> SEQ ID NO 101

<211> LENGTH: 331

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 101

Ala	Ser	Leu	Phe	Ala	Leu	Ala	Ala	Cys	Gly	Gly	Glu	Pro	Ala	Ala	Gln
1				5					10					15	
Ala	Pro	Ala	Ala	Ser	Ala	Glu	Ala	Ala	Ser	Ser	Ala	Ala	Gln	Thr	Ala
		20						25					30		
Ala	Glu	Thr	Pro	Thr	Gly	Glu	Leu	Pro	Val	Ile	Asp	Ala	Val	Thr	Thr
		35					40					45			
His	Ala	Pro	Glu	Val	Pro	Pro	Ala	Ile	Asp	Arg	Asp	Tyr	Pro	Ala	Lys
	50					55					60				
Val	Arg	Val	Lys	Met	Glu	Thr	Val	Glu	Lys	Lys	Thr	Met	Glu	Asp	Gly
65				70						75				80	
Val	Glu	Tyr	Arg	Tyr	Trp	Thr	Phe	Asp	Gly	Asp	Val	Pro	Gly	Arg	Met
			85						90					95	
Ile	Arg	Val	Arg	Glu	Gly	Asp	Thr	Val	Glu	Val	Glu	Phe	Ser	Asn	Asn
		100						105					110		
Pro	Ser	Ser	Thr	Val	Pro	His	Asn	Val	Asp	Phe	His	Ala	Ala	Thr	Gly
		115					120					125			
Gln	Gly	Gly	Gly	Ala	Ala	Ala	Thr	Phe	Thr	Ala	Pro	Gly	Arg	Thr	Ser
	130					135					140				
Thr	Phe	Ser	Phe	Lys	Ala	Leu	Gln	Pro	Gly	Leu	Tyr	Ile	Tyr	His	Cys
145				150						155					160
Ala	Val	Ala	Pro	Val	Gly	Met	His	Ile	Ala	Asn	Gly	Met	Tyr	Gly	Leu
				165					170						175

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Ile Leu Val Glu Pro Lys Glu Gly Leu Pro Lys Val Asp Lys Glu Ser
      180                               185                               190
Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys Gly Lys Lys Gly Ala Gln
      195                               200                               205
Gly Leu Gln Pro Phe Asp Met Asp Lys Ala Val Ala Glu Gln Pro Glu
      210                               215                               220
Tyr Val Val Phe Asn Gly His Val Gly Ala Ile Ala Gly Asp Asn Ala
      225                               230                               235                               240
Leu Lys Ala Lys Ala Gly Glu Thr Val Arg Met Tyr Val Gly Asn Gly
      245                               250
Gly Pro Asn Leu Val Ser Ser Phe His Val Ile Gly Glu Ile Phe Asp
      260                               265                               270
Lys Val Tyr Val Glu Gly Gly Lys Leu Ile Asn Glu Asn Val Gln Ser
      275                               280                               285
Thr Ile Val Pro Ala Gly Gly Ser Ala Ile Val Glu Phe Lys Val Asp
      290                               295                               300
Ile Pro Gly Ser Tyr Thr Leu Val Asp His Ser Ile Phe Arg Ala Phe
      305                               310                               315                               320
Asn Lys Gly Ala Leu Gly Gln Leu Lys Val Glu
      325                               330

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<210> SEQ ID NO 102

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 102

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Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
  1           5           10           15
Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
  20           25           30
Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
  35           40           45
Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
  50           55           60
Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
  65           70           75           80
Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
  85           90           95
Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
  100          105          110
Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
  115          120          125
Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
  130          135          140
Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
  145          150          155          160
Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
  165          170          175
Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
  180          185          190
Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
  195          200          205
Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
  210          215          220

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Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240
 Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255
 Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270
 Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285
 Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290 295 300
 Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
 305 310 315 320
 Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335

Glu

<210> SEQ ID NO 103
 <211> LENGTH: 337
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 103

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1 5 10 15
 Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20 25 30
 Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35 40 45
 Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50 55 60
 Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65 70 75 80
 Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85 90 95
 Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
 100 105 110
 Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
 115 120 125
 Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
 130 135 140
 Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
 145 150 155 160
 Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
 165 170 175
 Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
 180 185 190
 Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
 195 200 205
 Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
 210 215 220
 Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240
 Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255

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Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270

Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285

Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290 295 300

Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
 305 310 315 320

Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335

Glu

<210> SEQ ID NO 104
 <211> LENGTH: 337
 <212> TYPE: PRT
 <213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 104

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1 5 10 15

Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20 25 30

Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35 40 45

Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50 55 60

Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65 70 75 80

Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85 90 95

Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
 100 105 110

Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
 115 120 125

Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
 130 135 140

Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
 145 150 155 160

Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
 165 170 175

Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
 180 185 190

Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
 195 200 205

Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
 210 215 220

Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240

Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255

Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270

Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285

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Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290                               295                       300

Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
305                               310                       315                       320

Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
      325                               330                       335

Glu

<210> SEQ ID NO 105
<211> LENGTH: 337
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 105

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1      5      10      15

Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20     25     30

Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35     40     45

Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50     55     60

Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65     70     75     80

Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85     90     95

Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
100    105    110

Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
115    120    125

Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
130    135    140

Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
145    150    155    160

Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
165    170    175

Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
180    185    190

Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
195    200    205

Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
210    215    220

Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
225    230    235    240

Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
245    250    255

Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
260    265    270

Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
275    280    285

Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
290                               295                       300

Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
305                               310                       315                       320

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Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335

Glu

<210> SEQ ID NO 106

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 106

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1 5 10 15

Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20 25 30

Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35 40 45

Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50 55 60

Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65 70 75 80

Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85 90 95

Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
 100 105 110

Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
 115 120 125

Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
 130 135 140

Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
 145 150 155 160

Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
 165 170 175

Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
 180 185 190

Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
 195 200 205

Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
 210 215 220

Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240

Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255

Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270

Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285

Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290 295 300

Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
 305 310 315 320

Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335

Glu

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<210> SEQ ID NO 107
<211> LENGTH: 337
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

<400> SEQUENCE: 107

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
1           5           10           15

Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
20           25           30

Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
35           40           45

Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
50           55           60

Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
65           70           75           80

Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
85           90           95

Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
100          105          110

Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
115          120          125

Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
130          135          140

Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
145          150          155          160

Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
165          170          175

Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
180          185          190

Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
195          200          205

Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
210          215          220

Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
225          230          235          240

Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
245          250          255

Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
260          265          270

Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
275          280          285

Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
290          295          300

Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
305          310          315          320

Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
325          330          335

Glu

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<210> SEQ ID NO 108
<211> LENGTH: 337
<212> TYPE: PRT
<213> ORGANISM: Neisseria meningitidis

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-continued

<400> SEQUENCE: 108

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1 5 10 15

Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20 25 30

Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35 40 45

Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50 55 60

Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65 70 75 80

Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85 90 95

Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
 100 105 110

Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
 115 120 125

Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
 130 135 140

Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
 145 150 155 160

Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
 165 170 175

Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
 180 185 190

Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
 195 200 205

Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
 210 215 220

Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240

Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255

Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270

Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285

Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290 295 300

Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
 305 310 315 320

Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335

Glu

<210> SEQ ID NO 109

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

-continued

<400> SEQUENCE: 109

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1 5 10 15
 Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20 25 30
 Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35 40 45
 Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50 55 60
 Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65 70 75 80
 Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85 90 95
 Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
 100 105 110
 Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
 115 120 125
 Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
 130 135 140
 Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
 145 150 155 160
 Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
 165 170 175
 Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
 180 185 190
 Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
 195 200 205
 Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
 210 215 220
 Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240
 Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255
 Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270
 Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285
 Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290 295 300
 Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
 305 310 315 320
 Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335

Glu

<210> SEQ ID NO 110

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

-continued

<400> SEQUENCE: 110

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1 5 10 15

Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20 25 30

Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35 40 45

Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50 55 60

Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65 70 75 80

Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85 90 95

Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
 100 105 110

Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
 115 120 125

Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
 130 135 140

Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
 145 150 155 160

Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
 165 170 175

Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
 180 185 190

Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
 195 200 205

Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
 210 215 220

Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240

Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255

Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270

Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285

Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290 295 300

Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
 305 310 315 320

Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335

Glu

<210> SEQ ID NO 111

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

-continued

<400> SEQUENCE: 111

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1 5 10 15
 Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20 25 30
 Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35 40 45
 Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50 55 60
 Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65 70 75 80
 Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85 90 95
 Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
 100 105 110
 Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
 115 120 125
 Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
 130 135 140
 Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
 145 150 155 160
 Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
 165 170 175
 Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
 180 185 190
 Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
 195 200 205
 Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
 210 215 220
 Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240
 Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255
 Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270
 Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285
 Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290 295 300
 Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
 305 310 315 320
 Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335
 Glu

<210> SEQ ID NO 112

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Neisseria meningitidis

-continued

<400> SEQUENCE: 112

Ala Ser Val Phe Ala Leu Ala Ala Cys Gly Glu Gln Ala Ala Lys Pro
 1 5 10 15

Ala Glu Thr Pro Ala Ala Thr Ala Ser Ala Glu Ala Pro Ala Ala Ser
 20 25 30

Asn Ser Gln Ala Ala Ala Glu Thr Pro Ser Ser Glu Leu Pro Val Ile
 35 40 45

Asp Ala Ile Val Thr His Ala Pro Glu Val Pro Pro Pro Thr Asp Arg
 50 55 60

Asp His Pro Ala Lys Val Arg Val Lys Met Glu Thr Val Glu Lys Thr
 65 70 75 80

Met Lys Met Asp Asp Gly Val Glu Tyr His Tyr Trp Thr Phe Asp Gly
 85 90 95

Asp Val Pro Gly Arg Met Ile Arg Val Arg Glu Gly Asp Thr Val Glu
 100 105 110

Val Glu Phe Ser Asn Asn Pro Ser Ser Thr Val Pro His Asn Val Asp
 115 120 125

Phe His Ala Ala Thr Gly Gln Gly Gly Gly Ala Ala Ala Thr Phe Thr
 130 135 140

Ala Pro Gly Arg Thr Ser Thr Phe Ser Phe Lys Ala Leu Gln Ala Gly
 145 150 155 160

Leu Tyr Ile Tyr His Cys Ala Val Ala Pro Val Gly Met His Ile Ala
 165 170 175

Asn Gly Met Tyr Gly Leu Ile Leu Val Glu Pro Lys Glu Gly Leu Pro
 180 185 190

Lys Val Asp Lys Glu Phe Tyr Ile Val Gln Gly Asp Phe Tyr Thr Lys
 195 200 205

Gly Lys Lys Gly Ala Gln Gly Leu Gln Pro Phe Asp Met Asp Lys Ala
 210 215 220

Ile Ala Glu Gln Pro Glu Tyr Val Val Phe Asn Gly His Val Gly Ser
 225 230 235 240

Ile Ala Gly Asp Asn Ala Leu Lys Ala Lys Ala Gly Glu Thr Ile Arg
 245 250 255

Met Tyr Val Gly Asn Gly Gly Pro Asn Leu Val Ser Ser Phe His Val
 260 265 270

Ile Gly Glu Ile Phe Asp Lys Val Tyr Val Glu Gly Gly Lys Leu Ile
 275 280 285

Asn Glu Asn Val Gln Ser Thr Ile Val Pro Ala Gly Gly Ser Ala Ile
 290 295 300

Val Glu Phe Lys Val Asp Ile Pro Gly Ser Tyr Thr Leu Val Asp His
 305 310 315 320

Ser Ile Phe Arg Ala Phe Asn Lys Gly Ala Leu Gly Gln Leu Lys Val
 325 330 335

Glu

<210> SEQ ID NO 113

<211> LENGTH: 4

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
 <223> OTHER INFORMATION: Carboxy-terminal serine-containing tetrapeptide
 repeat

<400> SEQUENCE: 113

Ala Ala Ser Ala

1

The invention claimed is:

1. A method of eliciting an immune response to a bacterial pathogen of the genus *Neisseria* in a host, said method including the step of administering to said host an immunogenic composition comprising an isolated mutant *Neisseria* nitrite reductase polypeptide that is not glycosylated, wherein the mutant *Neisseria* nitrite reductase polypeptide comprises an amino acid sequence lacking a carboxy-terminal serine-containing tetrapeptide repeat AASA (SEQ ID NO: 113) of a corresponding wild-type *Neisseria* nitrite reductase glycoprotein and elicits a more immunologically effective immune response compared to the corresponding wild-type *Neisseria* nitrite reductase glycoprotein, to thereby elicit an immune response to said bacterial pathogen in said host.

2. The method of claim 1, wherein said host is a mammal.

3. The method of claim 2, wherein said host is a human.

4. The method of claim 1, wherein the immune response prophylactically or therapeutically treats an infection by a bacterial pathogen of the genus *Neisseria*.

5. The method of claim 4, wherein said bacterial pathogen is *Neisseria meningitidis* or *Neisseria gonorrhoeae*.

6. The method of claim 1, wherein the isolated mutant nitrite reductase polypeptide comprises an amino acid sequence selected from SEQ ID NOs: 1-4 or 6-8.

7. The method of claim 1, wherein the immunogenic composition further comprises a carrier, diluent or excipient.

8. The method of claim 6, wherein the isolated mutant nitrite reductase polypeptide consists of the nitrite reductase polypeptide amino acid sequence of any one of SEQ ID NOs: 1-4 or 6-8.

9. The method of claim 1, wherein the isolated mutant nitrite reductase polypeptide further lacks an N-terminal amino acid sequence of the corresponding wild-type polypeptide.

10. The method of claim 1, wherein the carboxy-terminal serine-containing tetrapeptide repeat AASA (SEQ ID NO: 113) is located within amino acids 355-390 of SEQ ID NOs: 31-34, 74, or 75.

* * * * *